CONSIDERATIONS WHEN SELECTING A CRO FOR PHASE I CLINICAL STUDIES

INTRODUCTION

Phase I clinical trials are an integral step in the drug development process. Specific factors can influence the timelines and success of these studies, including,

- Clinical, therapeutic, medical and regulatory experience
- Efficient processes and access to study participants
- An infrastructure and processes that mitigate risk
- Modern, efficient facilities.

This white paper addresses the critical success factors for Phase I clinical studies and provides guidance on the appropriate capabilities, expertise and experience to evaluate as a sponsor selects a CRO.

EXPERIENCE

One of the most important considerations in the CRO selection process is broad experience in Phase I trial execution. An organization with solid a track record of providing services from protocol design to final study reporting possesses the expertise to streamline execution. This can help sponsors shorten timelines for quicker go/no-go decisions.

Broad exposure to different types of studies, therapeutics and dosage forms are also pivotal in developing protocols to meet the varied needs of each sponsor. Creative and innovative study design for first in human, proof of concept, drug interaction, single ascending dose/multiple ascending dose (SAD/MAD) and cardiac safety studies are essential for ensuring safe and efficient study conduct.

Finally, a record of working with regulatory agencies world wide and significant experience filing clinical trial applications is critical to the successful completion of your study.

EXPEDITED PHASE I STUDIES

There are three contributing factors to a Company's ability to expedite Phase I studies

- The ability to rapidly recruit study participants,
- The capability to efficiently conduct clinical trials
- Rapid data collection and analysis tools

RAPID RECRUITMENT

The ability to provide rapid and efficient recruitment and access to a broad population is vital to meet or improve upon project timelines. An extensive centralized database and access to a significant population of potential participants is critical to a successful recruitment process. The ideal database will contain a diverse group of both normal healthy volunteers and patients that fit the required special populations.

The ability to proactively and effectively respond to complex recruitment challenges with novel strategies for wide range of study criteria is also required.

STREAMLINED OPERATIONS THROUGH EFFECTIVE STUDY DESIGN

Effective study design starts with a protocol that includes all of the study parameters and will focus on improved study efficiency, better data and shorter timeframes. Once the protocol is accepted, a knowledgeable team can streamline execution of the study. The ability to communicate the best strategies is an important part of the process to ensure sponsors understand their options. Another frequent strategy is to run SAD/MAD studies in a single trial to reduce timelines.[1]

There is also an increased interest in obtaining more cardiac safety information (QT data) as part of the FIH study. Since Phase I studies are designed to identify the maximum tolerated doses, the effect on the QT interval can be assessed during SAD/MAD studies at doses that are often much higher than those that could be studied in a formal, thorough QT study. Earlier detection of a cardiac safety issue can lead to conducting a thorough QT study much earlier in the clinical development process or to earlier termination of a program, thereby saving time and money.[2]

FASTER, HIGH QUALITY DATA MANAGEMENT

During the course of the study, the ability to rapidly and accurately handle data in a rapid manner is critical. Bar coding for sample tracking, robust clinical trial management software (CTMS) and access to electronic data capture (EDC) capabilities reduces potential errors and data verification time, permitting near real-time, transcription-free data access. A best in class biostatistics/pharmacometrics team should analyze the data

[1-2] Mario Tanguay's "Phase I Efficiency" from *International Clinical Trials* May 2010 (footnote data to come)

using automated and validated systems for rapid compilation of the clinical study report.

MITIGATING RISK THROUGH INFRASTRUCTURE AND PROCESSES

In combination with experience and the ability to expedite studies, sound processes helps mitigate risk. This includes the availability of a team of professionals to provide counsel on the potential risks in the study and how to avoid them, contingency plans, open and frequent communication processes, and robust quality and regulatory controls to ensure compliance and patient safety.

PROJECT MANAGEMENT EXPERTISE

Central to mitigating risk in clinical studies is a knowledgeable team of professionals from business development, clinical operations, and medical, scientific and regulatory affairs.

Communication processes starts with an experienced business development professional who works closely with the project manager to initiate the contract process, convey sponsor requirements and oversee communications.

The project manager for your trial should ensure the study will be executed on time and within the scope of the requirements. Project managers should have the authority to schedule the necessary resources, resolve issues, and manage critical milestones and deliverables to ensure the project stays on track.

The clinical operations team should include a wide range of medical professionals such as doctors, nurses, medical technicians and clinical research monitors in order to provide the safest environment for the study participants during the trial. Access to experienced staff in cardiac safety and drug interactions is important when dealing with more complex trials. On-site physicians and medical professionals should monitor each study to ensure the safety of volunteers.

Scientific and regulatory affairs experts should be available to collaborate throughout the study in the assessment of overall feasibility, protocol development, bioanalytical and clinical feasibility, recruitment planning and screening, institutional review board presentation, and regulatory submission.

PROCESS EXCELLENCE

Aligning processes to assist sponsors in managing risk in the early stage process requires years of experience in conducting Phase I trials. In the earliest stages of developing the protocol, risk management has to be a consideration. By making these plans upfront, the CRO can reduce the chances of losing momentum during the study.

Providing robust quality and regulatory controls throughout the entire study will promote compliance. Quality assurance processes, including internal training programs, auditing vendors, validating software and establishing SOPs, indicate that the CRO that is committed to providing high quality.

Established processes to ensure the safety of study participants is one of the most important considerations when selecting a CRO.

MODERN AND EFFICIENT FACILITIES

The clinical facility should have the capacity to conduct multiple studies simultaneously and a variety of study types and house qualified participants.

Ensure there are the necessary special handling capabilities in the pharmacy, particularly if dealing with controlled substances or specific storage conditions. There should be restricted access to this area to ensure patient safety and accurately maintain an audit trail. Evaluate the availability of any specialized equipment that is needed such as refrigerators, freezers and laminar flow hoods that may be necessary for the storage, dispensing and preparation of certain drugs.

SUMMARY

Selection of the best CRO can trim study time, costs and risk from the pharmaceutical development process while obtaining quality results that enable solid business and scientific decisions. A CRO with the right talent, technology, systems, and procedures can provide meaningful benefit to a sponsor's development program.

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