Clinical Trials 101

Is clinical research a good fit for your practice?

BY AVNER INGERMAN, MD, MSc; CIERA MAFFEI; AND DAVID WATERS-HONCU

Do you have what it takes to participate as a site in a clinical trial? What are the requirements to qualify as a site and what kind of commitment will participation entail? These are just a few of the questions that we will answer in Retina Today's *newest column,* Clinical Trials for the Retina Specialist.

—Avner Ingerman, MD, MSc

Retina specialists rely on clinical trials to answer clinical and medical questions, as well as those related to safety and efficacy of therapies and the natural course and causes of diseases. Clinical trials involve patients who voluntarily participate in these trials, and the commitment of these patients, their families and caretakers, cannot be appreciated enough. Their efforts help increase our knowledge base, guide our medical decision-making, and benefit our patients and the medical system.

The presentation of data obtained in a clinical trial is the pinnacle of a long and often expensive effort. This effort is a complicated project that involves many individuals, groups, and organizations, many of whom work behind the scenes. This article is an introduction to the main characters in clinical trials.

PROTOCOL: THE SCREENPLAY

The protocol is the roadmap, or screenplay, of a study. This intricate document explains the background and study rationale, sets forth efficacy and safety endpoints, defines the target number of subjects to be studied, details inclusion and exclusion criteria to identify participants fitting the target study population, outlines study procedures and order of assessments, discusses the intervention, includes statistical analysis plans, and details adverse event reporting guidelines. Study sponsors, contract research organizations (CROs), institutional or independent review boards (IRBs), data management, reading centers, and central laboratories are all involved in retinal clinical trials and may have a hand in protocol development.

The protocol is of unique importance because it defines precisely the exact steps and procedures that must be conducted at every study visit. The goal of the protocol is to create a standard approach to allow a statistical power of analysis. Many clinicians find it difficult to strictly follow a set protocol because they are trained to make their own judgments and clinical evaluations and decide on the use of diagnostic tools and treatment options. In many ways, the protocol limits these freedoms by mandating actions at each visit. However, it is important to understand that a clinical trial demands a greater need for a standard approach to procedures and evaluations to generate a scientific statistical analysis of the data compared with everyday clinical practice.

PLAYERS BEHIND THE SCENE

The study sponsor is the party funding the research, and this entity is in many ways the "owner" of the protocol and its design. CROs provide a service to the sponsor and often manage the conduct of clinical trials. CROs are also likely to facilitate regulatory relations regarding the protocol and other aspects of the study.

The IRB conducts regulatory and ethical reviews of study materials and ongoing study issues. IRBs may exist within specific institutions (hospital IRBs) or be independent entities. IRB approval of all study materials is required prior to conducting study procedures.

Data management groups are charged with properly compiling and handling the plethora of data generated for the study participants. Reading centers provide centralized evaluation of retinal imaging outputs, such as digital angiographic images,[1] and central laboratories provide centralized laboratory assessment, such as blood chemistry or electrocardiogram readings.

PLAYERS AT THE SITE

The site is where the study takes place. In the retina world, the site is often the office of the retina specialist. The treating doctor and the patients follow the study protocol.

The principal investigator (PI) is responsible for the study conducted at his or her research site. While staff members

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and subinvestigators may conduct certain procedures, the PI has overall responsibility for oversight of all duties.

The study coordinator, or clinical research coordinator, is responsible for managing the daily operations at a particular site. Duties often include interaction with the CRO, the sponsor, central laboratories, monitors, and study subjects, as well as managing study logs (adverse event reporting and follow-up, protocol deviations, etc.) and performing other tasks (data entry, case report forms) as applicable.[2,3] Many sites conducting retinal clinical studies have dedicated study coordinators within research departments whose sole responsibility is to conduct studies. This is a role that requires dedication, attention to detail, and a multitasking skill set.

Monitors, often called clinical research associates, are individuals from either the sponsor or CRO who visit the study site periodically to review collected data, perform quality assurance checks, and gauge the study's progress.

Auditors are responsible for examining data collection and study conduct to assure subject safety and compliance. Auditors may be representatives of the sponsor, the IRB, or regulatory authorities, such as the US Food and Drug Administration (FDA). Sponsor audits are sometimes mock FDA audits. In this scenario, the auditors will follow the FDA manual for inspection plan.[4] Audits are a routine practice to ensure that the site is conducting studies correctly, that the protocol is followed properly, and that the data are captured with the required quality. Audits may also be "for-cause" audits, with the purpose of vetting an ethical or regulatory compliance concern. FDA audits are conducted to determine validity and integrity of the data, to assess regulatory adherence, and to ensure that rights and safety of human subjects are properly protected.[5]

CONCLUSION

Many organizations and individuals are responsible for organizing and executing a clinical trial. Next month's article will discuss specifically how a trial is set up. ■

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