Attributes of Exemplary Research

Implementing Clinical Trials: A Review of the Attributes of Exemplary Clinical Trial Sites

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Introduction

Conducting clinical research is an integral part of cancer care and treatment advances. In 2008, ASCO published the Statement on Minimum Standards and Attributes of Exemplary Clinical Trial Sites to address the minimum requirements of sites conducting quality clinical trials and the attributes of exemplary sites.[1] Both the minimum requirements and exemplary attributes were based on a review of the literature, current regulatory requirements, and consensus among community and academic clinical researchers. After publication of the Statement, ASCO developed several initiatives to assist research sites in developing and maintaining exemplary research programs. These initiatives include award and grant opportunities through the ASCO Cancer Foundation,[2] the Exemplary Attributes article series published in *Journal of Oncology Practice* (*JOP*)[3] and development of a Web page (www.asco.org/ClinicalTrialResources) that links to helpful clinical trial resources.

Most recently, at the 2010 ASCO Annual Meeting, members from the Exemplary Attributes Working Group presented an extended education session on the implementation of clinical trials. The session can now be viewed online through ASCO Virtual Meeting and is entitled, "Implementing Clinical Trials: Risks, Benefits, Marketing and Paying for It All."[4] On the basis of the positive feedback from this session, the faculty has chosen to review some of the session's content in a two-part series of articles. Although numerous topics were covered in the session, these two articles will specifically focus on the seven attributes of exemplary clinical trial sites, as stated in the ASCO Statement: (1) diversification of the clinical trial mix, (2) high accrual activity, (3) participation in the clinical trial development process, (4) maintenance of high educational standards, (5) quality assurance, (6) multidisciplinary involvement in the clinical trial process, and (7) clinical trial awareness programs.

Diversification of the Clinical Trial Mix

Offering a broad range of clinical trials ensures that patients have the best research options available to them. Diversification of the clinical trial mix also makes greatest use of a site's research infrastructure and resources. A site wishing to increase diversity of its portfolio may offer trials studying different disease stages, agents in different phases of development, or cancers that are rare or have specific genotypes. A diverse portfolio may also include trials studying questions related to prevention and supportive care. Regardless of the type of trials selected, it is most important to choose trials that are scientifically compelling and address the current needs of patients. This ensures that patients will receive the best possible care and simultaneously that the study will make significant contributions to cancer research.

A site considering which trials to include in its portfolio should select the trials most appropriate for its population. Considering unique features of the community's patient population will help the research team determine how these will influence the population's eligibility for certain trials. Factors such as age, disease stage, and presence of comorbidities will determine whether patients are eligible for certain trials. Considering and evaluating the potential impact of these factors in advance of opening a new trial limits ineffective expenditure of resources on trials that are unlikely to accrue at the site.

In developing its portfolio, a site should consider trials in which a patient may enroll simultaneously or in succession. For example, a patient enrolled onto a therapeutic trial may also have interest in participating in a quality-of-life or correlative science trial. Likewise, a patient who experienced a disease relapse after primary treatment through a clinical trial may be interested in pursuing secondary treatment through a clinical trial studying a different agent. In certain settings, it may also be beneficial to offer clinical trials onto which patients' family members can enroll, such as prevention trials or biologic correlative studies. Analyzing the population served by the site, including demographics and cancer-specific prevalence, will help the research team determine which trials are most likely to be successful.

A diverse research portfolio can also ensure financial sustainability of the research program. Many sites achieve a cost-neutral research program by offering both government-sponsored and non–government-sponsored trials.[5] Investigators find value in conducting government-sponsored trials but often find that these trials pay the research site less than the actual cost the site incurs.[6] A strategy used to overcome this barrier is offering trials through private sponsors, such as companies conducting clinical trials related to therapeutic agents, devices, or products related to supportive care. Private sponsors usually provide reimbursement more closely aligned to the site's cost than do government sponsors.

The ability to offer a diverse portfolio of trials often evolves with the growth of a research program. New research programs may choose to offer a select number of trials that will accrue patient

populations seen in high volume at the site. Once the program becomes more established, the research team might then begin to increase the diversity of trials offered at the site. Offering cancer control studies is also a good choice for a young research program. Cancer control studies, such as prevention and quality of life studies, often answer valuable questions and generally can be conducted in one patient encounter. These trials may include collecting blood samples to be stored in a biobank or conducting a patient survey regarding pain or fatigue. These trials help give the research team experience working with the institutional review board (IRB), conducting informed consent, and recording and reporting patient outcomes. Participation on these trials is also a requirement for sites that are part of the National Cancer Institute's Community Clinical Oncology Program.[7]

High Accrual Activity

According to the ASCO Statement on Minimum Standards and Attributes of Exemplary Clinical Trial Sites, exemplary clinical trials sites should accrue at least 10% of the patients treated at the site onto clinical trials.[1] However, the ASCO Statement also suggests that the research team determine site-specific accrual goals based on a site's demographics and cultural perspectives. On the basis of this analysis, the site-specific accrual goal may be greater or less than 10%. Once this goal has been established, a site should monitor itself for achieving the accrual goal and consider interventions to promote accrual. Ideally, a site would continuously aim to maintain or even raise the standards for accrual and implement interventions, such as diversifying the clinical trial portfolio, to achieve maximal accrual. Regardless of the site's exact goal, research teams should always aim to have the highest accrual activity possible for their site.

There are many ways a research team can promote high accrual. One way is to activate new trials in a timely manner, thus providing a site more time and opportunity to accrue patients onto the trial. Because initial trial implementation can cost several thousand dollars, opening a trial that is unlikely to accrue at the research site may result in a financial loss for the site.[8] This is also true of trials that are about to close, because they result in inadequate time to enroll patients. When opening a multicenter trial, a site should review the national accrual data and the projected closure date to predict trial accrual success at the site. In addition, if trial implementation is being delayed because of the IRB approval process, the research team should work with the IRB to determine ways to facilitate efficiency. There are many opportunities for the research team to facilitate efficient IRB reviews, such as responding to IRB questions in a timely manner or giving consideration to utilizing the central IRB when opening multicenter trials sponsored by the NCI.[9]

Most important, high accrual activity requires that clinical research be embedded into the culture of the site. This culture can be promoted in a number of ways, including designation of "physician champions" who are committed to research, actively promote clinical research at the site, and engage their colleagues and staff. These individuals should work to instill in their team the principle that every patient should be considered for participation in a clinical trial. This approach is in keeping with National Comprehensive Cancer Network (NCCN) guidelines, which state that "The NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged."[10] Even if the patient is not eligible to enroll onto a therapeutic trial, the patient might be interested in participating in a cancer control trial or donating biospecimens for research. For this reason, physicians should talk to every patient about the significance of clinical research for determining current cancer care interventions. Recognizing that speaking to patients about clinical research may require more time than educating about standard treatments alone, a research program should be organized in a manner that enables this to occur in the most efficient manner possible. Research staff members should be designated to conduct certain tasks on the basis of their position and capabilities. For example, a research associate may conduct chart reviews to screen patients potentially eligible to enroll in a certain trial, or the physician may introduce a clinical research trial to a patient and then have the research nurse provide additional education and contribute to the conduct of the informed consent process. Delegating tasks to various members of the research team makes clinical trial accrual a more manageable task.

Sites may also promote accrual by engaging populations who are underrepresented in research trials being offered at the site. A site might wish to conduct a gap analysis to analyze the demographics of patients treated at the site and compare this information to the demographics of patients enrolled onto clinical trials. If a gap is apparent, the team should evaluate why the gap exists and develop interventions for engaging the population. Working with local support groups and institutional groups serving these populations may serve as a mechanism to evaluate and overcome local barriers to care.

Sites should also monitor accrual to each trial and evaluate any trials that are not accruing at an acceptable level. Depending on the evaluation, it may be appropriate to implement a corrective action plan. In other cases, such as when the trial no longer represents the most current science in the field, it may be in the best interest of the site to close a nonaccruing trial. A site can gain helpful insight related to the science of trial accrual by reviewing abstracts and resources from the NCI-ASCO Cancer Trial Accrual Symposium. These materials are freely available to the public online.[11]

Participation in the Clinical Trial Development Process

According to the ASCO statement, "Active collaboration between the community practice, an affiliated academic center, and the trial sponsor can be instrumental in the development and implementation of clinical trials."[1] This collaboration helps ensure that protocols will be both scientifically compelling and reasonable to implement in the community setting. Ease of implementation at community sites is vital to the success of a trial, as this is where approximately 50% of patient accrual to clinical trials occurs.[1]

There are various opportunities for researchers and their staffs to participate in the trial development process. Researchers might volunteer for committees related to clinical trials; attend research meetings conducted by the trial sponsor; author research protocols or journal articles; or assume leadership roles, such as serving as a

principal investigator on a trial. Participation ensures continued engagement of investigators and staff while also providing an important contribution to cancer research.

Maintenance of High Educational Standards

Maintaining high educational standards is of utmost importance to investigators and research staff for promoting the conduct of high-quality research. Investigators practicing in the United States are encouraged to become specialty board certified, and investigators working in countries that do not provide an option for certification are encouraged to maintain high educational standards at a level similar to what is required locally. Regardless of where an investigator is practicing, it is important to stay engaged and current on issues in the field.

Mechanisms of maintaining high educational standards include participating in continuing medical education activities, attending meetings conducted by trial sponsors, regularly reading scientific publications, attending meetings and symposia, and participating on local tumor boards. Numerous educational opportunities are also available online, including options provided through ASCO.[12]

Research staff must also be educated. At a minimum, staff should receive training appropriate to their position, as required by Good Clinical Practice regulations and guidance. Staff may also pursue certification applicable to their position. Education and certification may be pursued through organizations such as the Society of Clinical Research Associates[13] or the Association of Clinical Research Professionals.[14] When implementing a research program, a site should take into account the time and cost associated with maintenance of high educational standards and should implement a policy for monitoring compliance and ensuring appropriate maintenance of staff licensures and certifications.

This article provides an overview of four of the seven attributes of exemplary clinical trial sites and suggests ways for a site to implement these attributes. The remaining three attributes, quality assurance, multidisciplinary involvement in the clinical trial process, and clinical trial awareness programs, will be discussed in the next article in the series.

Feedback Request

Suggest future topic ideas for the series and provide your feedback by sending an e-mail to researchresources@asco.org.

Implementation of one, or all, of the attributes will help a site develop well beyond the minimum Good Clinical Practice requirements and ultimately lead to a stronger research program. Research sites interested in receiving funding to assist with the implementation of the exemplary attributes are encouraged to pursue the Community Oncology Research Grant offered through the ASCO Cancer Foundation.[2]

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