Minimizing Research Delays: Identifying Successful Strategies to Keep a Clinical Trial Moving Forward

Left to right: Allen S. Lichter, MD, ASCO Executive Vice President; Louis Fehrenbacher, MD, Oncology Clinical Trials Program, Kaiser Permanente, Northern California; and Gabriel N. Hortobagyi, MD, ASCO Immediate Past President.

Once the decision has been made to participate in a clinical trial, clearly it is important to minimize research delays to keep that trial moving forward. Representatives of several practices that were recognized by the American Society of Clinical Oncology (ASCO) by presentation of its 2007 Clinical Trials Participation Awards, have identified successful strategies they have developed to keep the clinical trials they conduct on track. These strategies include ways to work with their institutional review boards (IRBs), identify and accrue eligible patients, identify roadblocks before they happen, and assure participant compliance and data validity. The practices sharing their strategies include the Cancer Research and Support Services of Summa Health System, Oncology Clinical Trials/Duluth Community Clinical Oncology Program (CCOP), Oncology Clinical Trials Program, Kaiser Permanente, Northern California, Oncology Hematology Care Inc, and the Department of Pediatric Hematology/Oncology at the University of Texas Health Science Center at San Antonio/Christus Santa Rosa Children's Hospital.

Working With IRBs

Oncology Hematology Care (OHC) Inc uses an external, commercial IRB for clinical trial oversight, but according to Ann Bradley, OHC Research Program Coordinator, Oncology Hematology Care Inc, Cincinnati, Ohio, this is "not a big problem." The other award-winning practices use internal or central IRBs. Louis Fehrenbacher, MD, Oncology Clinical Trials Program, Kaiser Permanente, Northern California, Vallejo, California, says that their research group is well aware of what their central IRB will look for when they are considering a new trial, including what is acceptable wording for patient consent forms as well as what constitutes

approvable contents for other documents. The research group strives to get things right the first time to avoid delays. They also use the National Cancer Institute central IRB for phase III cooperative group trials, but they don't use commercial external IRBs. "We're not allowed to work with external IRBs," says Anne Forsman, BSN, RN, OCN, Manager, Oncology Clinical Trials/Duluth CCOP, Duluth, Minnesota. "We have opened two trials with a central IRB, but because our IRB hasn't grasped the concept, it almost doubled our work." The Children's Oncology Group at the University of Texas Health Science Center at San Antonio/Christus Santa Rosa Children's Hospital, Department of Pediatric Hematology/Oncology, San Antonio, Texas, has hired a regulatory specialist dedicated to handling the cancer protocol submissions to their IRB, says Paul Thomas, MD. This was in response to changes at the university that eliminated an electronic IRB approval process that had been used for some of their protocols. Another clinical research associate handles their hematology research efforts.

Accrual and Patient Databases

For the last 2 to 3 years, Kaiser Permanente has used its electronic database to identify patients eligible for clinical trials. Fehrenbacher says that their large patient population of 3.3 million members in Northern California and the informatics they have available to search their patient database contribute to their success. "It's a more efficient and comprehensive alternative to running ads in the paper or educating referring physicians to identify patients," he observes. "We get a more population-based cohort that is more representative because the program is so large." He notes that their practice has the third highest accrual in the country for the Study of Tamoxifen and Raloxifene (STAR) trial, and that their extensive electronic database helped enormously to achieve it.

The patient population the Duluth CCOP reaches out to about 450,000, and draws from northeast Minnesota, northern Wisconsin, and part of the upper peninsula of Michigan. Research assistants screen all new patients going into the practice. "They used to look at paper charts," says Forsman, "but we have electronic records now." Formerly they relied on print advertising and a lot of radio advertising to recruit. Once patients have a diagnosis, the day before their appointments a list of the trials they may qualify for is generated. Although their studies include symptom management and cancer control trials, for which it is more difficult to prescreen patients, a cancer control nurse tries to screen all patients coming into the clinic each day to see if a trial would fit.

At Summa Health System, Akron, Ohio, the patient databases are currently half electronic and half paper, says Joyce Neading, RHIT, CTR, Manager, Cancer Research and Support Services. "When a patient comes in to consult, we have computer access to pathology, radiology, and biopsy reports. If the patient has a malignancy and there is an appropriate trial, we notify the physician that the patient is a likely candidate." Early on the day of the patient's visit, the physician will present the concept of trial participation in general terms. It is the role of a nurse to explain the protocol and treatment in detail. The nurse will also discuss the consent form, which is sent home with the patient along with the nurse's business card. The nurse calls the patient within a couple of days to follow-up. Neading says that this process reduces the drop-out rate. Patients are told up front that if they feel strongly about receiving a particular treatment and won't accept random assignment, they shouldn't enroll in the trial. "Nurses do a good job presenting to patients. They sit and answer questions, it could be one to two hours, and they could meet more than once. That time is time well spent," Neading concludes.

Identifying Possible Roadblocks Before They Happen

At Kaiser Permanente, Carol P. Somkin, PhD, Senior Research Scientist, Division of Research, has an RO1 National Institutes of Health grant to evaluate their participant identification system and to increase enrollment rates. For six to eight clinical trials, potentially eligible trial participants will be identified through their pathology reports in the electronic records. Half of the patients will be contacted by a research nurse and will receive explanatory material about clinical trial participation by mail, allowing patients to review material and discuss it with their family before they see their oncologist. "We think this is pretty innovative," Fehrenbacher says. He notes that because all of their patients are within one health care program, contacting potential trial participants this way is in compliance with the Health Insurance Portability and Accountability Act. Desiree Goldstein, RN, Oncology Clinical Trials Program, Kaiser Permanente, notes that whereas cooperative groups may audit trials in 3-year cycles, Kaiser Permanente conducts its own audits to ensure adherence to the protocols. She notes that access to information for both patients and physicians is a key to preventing roadblocks in a practice where the physicians have no dedicated research time outside of their clinic responsibilities.

Forsman says that until last year they had a clinical research assistant travel to their sites to assist the physicians in screening outreach patients, but that individual had to be "pulled back to the mother ship" due to lack of funding. She says that it was most successful in getting physicians who usually didn't put patients on trial to enroll them. One problem is that physicians at the outreach sites may see as many as 35 patients a day in the clinic and don't have

separate time for their clinical trial work. Therefore, identification ahead of time of potentially eligible patients at the outreach sites is helpful. An even more important strategy in preventing roadblocks is the presence of two reimbursement specialists in the main cancer center and a recently hired manager for the outreach area. Their biggest role is to work with insurance companies to make sure that the center receives reimbursement for chemotherapy used on trial. "We do have what we consider to be a fairly high denial rate, maybe because we are asking the question, and others may not be telling the insurance company that the patient is on trial," she observes. Their in-house specialists are required to work with the insurance company as soon as a patient is considered for clinical trial participation.

Assuring Trial Participant Compliance and Data Validity

Goldstein points out that ensuring compliance starts with informed consent, clearly explaining patients' responsibilities and requirements at the outset, and getting them to agree to adhere to the protocol. Frequent patient contacts also ensure compliance. "If patients come in only at three to six month intervals for their oral medication, we contact them monthly to make sure they are taking the correct dose. We don't have a problem with patients dropping out of studies. Some elderly patients appreciate getting phone calls that someone cares about them." At Kaiser Permanente, research nurses follow patients closely in "real time," using the electronic records system to ensure that patients comply with scheduled visits, blood work, and other diagnostic tests. Alert sheets listing 10 to 15 potentially confusing aspects or pitfalls in a trial are put in the patient's chart to help ensure compliance.

Fehrenbacher notes that the Kaiser Permanente patient population on clinical trials has been well studied and does reflect the general population. He notes that when patients are self-referred or referred by tertiary treatment centers, the population tends to be younger and of higher socioeconomic status, making it harder to extrapolate results.

Summa provides patients with calendars and road maps of their whole treatment, and these are updated regularly, helping patients plan, according to Neading. Data management nurses participate on a daily basis, making sure required tests are done. Nurses fill out the case report forms and meet with patients until the follow-up visit. Research assistants are responsible for long-term follow-up. Neading says that it is extremely rare for a patient to be lost to follow-up. At the end of a trial, patients can sign a form consenting to follow-up or refusing it. Neading observes that it takes a lot of time and patience to explain trials to potential participants. The time their patients spend with the nurses results in a relationship that she believes helps to keep their patients on study.

DOI: 10.1200/JOP.0764002