Efforts To Communicate Clinical Trial Results to Patients Face Uphill Climb

By Karyn Hede

In the post-Vioxx era, clinical researchers are beginning to embrace openness and greater transparency in an effort to restore patient confidence. Awareness campaigns and publicly accessible clinical trials registries are a few of the new efforts to improve the public perception of clinical trials. But a few would-be reformers are suggesting another way to boost public confidence: Offer clinical trial participants the opportunity to be told their outcome.

“There is a lot of suspicion about clinical trials and what they represent,” said Antonio Wolff, M.D., associate professor of oncology at Johns Hopkins Kimmel Cancer Center in Baltimore. “By offering results, we are empowering patients and reinforcing to them and to their family and friends the individual and societal value of clinical research. That could indirectly, by word of mouth, have a positive impact on recruitment.”

Wolff has begun a conversation among members of the American Society of Clinical Oncology’s health services committee, which he chairs, designed to jump-start the practice of sharing research results.

“I think we do a wonderful job in spending time with patients with the informed-consent process, but after the active portion of the study is over, that is the end of our relationship with that patient,” Wolff said. “What we do by coming back to the patient at the end is saying, ‘We value your effort in volunteering your time and yourself to be in a clinical study.’ We are saying that, ‘What you’ve done is so important that we’d like to give you individually firsthand, should you want it, the outcome of the study.’”

While the idea seems simple, it is not part of the culture or expected practice in clinical trials, said Nancy Kass, Sc.D., a bioethicist at Johns Hopkins University who served on the National Cancer Institute’s central institutional review board.
and helped develop informed-consent documents for NCI-sponsored cancer clinical trials. But that can change, as it has with informed consent. Forty years ago it was common to enroll patients in clinical trials without their knowledge, she said. Over time, institutional review boards and informed consent became an accepted and legally required part of the system, but Kass said that because reporting results to patients was not required, it did not become common practice. That attitude is now changing, she said.

For example, the National Cancer Cooperative Groups, which enroll more than half of patients in U.S. cancer clinical trials, has established guidelines for disclosure of clinical trial results to patients enrolled in its studies and issued recommendations on how to communicate with patients if trials close early for any reason. They suggest that the treating physician (or the physician’s designee) tell the trial participant the reason for the closure, the potential consequences of the closure for the patient’s health, and any changes in treatment or follow-up required as a result of the new information.

But these guidelines are the rare exception. In practice, physicians often do not share trial results, even when trials are closed for fraud. In a recent highly publicized case, NIH researcher Trey Sunderland, Ph.D., was accused of misconduct by, among other things, inappropriately transferring to Pfizer Inc. more than 3,200 samples of spinal fluid collected for Alzheimer disease research. The long-term studies have been halted in the wake of the scandal, and yet patients who enrolled in the studies have had little communication about the status of the research.

**Why Doctors Don’t Share Data**

In one of the few studies of oncology physicians and nurses attitudes about sharing research results (J Natl Cancer Inst 2004;96:629–32) physicians reported a willingness to share research results (80%), but in practice they rarely shared results (62% shared results less than one-fifth of the time). They also voiced concerns about sharing research results with patients, with 60% fearing the emotional impact on participants.

Recent research suggests that their concern is well founded, according to Ann Partridge, M.D., a breast cancer oncologist at Dana-Farber Cancer Institute in Boston who studies patients’ reactions to receiving results from their clinical trials. At the 2006 American Society of Clinical Oncology meeting, Partridge reported patients’ reactions to results of NCCTG 9831, a phase III trial of adjuvant chemotherapy with or without trastuzumab for women with HER2+ breast cancer. Women who received trastuzumab reduced their risk of recurrence by 52% compared with those getting chemotherapy alone; the risk reduction was unrelated to age, hormone receptor status, tumor size, or lymph node involvement. Partridge said she chose this group because she...
wondered whether patients who had not received trastuzumab would have anxiety about their risk of recurrence when told the result. The research team sent surveys to all 228 trial participants and received responses from 160. Nearly all respondents reported that they were glad to have received the information, with 81% of the women satisfied with how results were shared. However, 63% of women reported that learning the results affected their lives, with 24% saying the results made them more anxious about their health. The study suggests that patients want results, she said, but investigators ought to think carefully about the impact that learning results, particularly negative results, could have on patients.

“It’s not a no-brainer,” she said. “I think it’s the right thing to do, but I think it’s something we have to do carefully.”

Wolff said there are already excellent examples of how to inform patients of trial results. He points to the MA.17 clinical trial, which tested whether extended adjuvant therapy with the aromatase inhibitor letrozole after tamoxifen reduced the risk of breast cancer recurrence. The trial was halted early after an interim analysis showed that letrozole improved disease-free survival (J Natl Cancer Inst 2005; 97:1262–71).

Study coordinators sent out a mass e-mail to study sites 3 days before publicly announcing that the trial was being stopped. The notice included a memo to patients including information that all enrolled patients would be offered open-label access to letrozole. The advance notice allowed Wolff’s research nurse to contact all patients enrolled at Hopkins and answer any questions before the results became public.

Wolff said the medical community is often skeptical of major changes to accepted practice, and more research may be needed to convince clinicians that giving patients results of clinical trials can be done without unduly burdening the system.

But patient advocates say the process does not have to be complicated. Physicians and trial sponsors often project expectations onto patients, and simple steps can be taken to keep patients informed.

“There is this perception that any communication about a trial is taboo,” said Ken Getz, cofounder of the Center for Information and Study on Clinical Research Participation, Dedham, Mass., a nonprofit organization that studies clinical trial participation. “There is enough evidence to suggest that there are things we can do now to communicate to volunteers who are eager to just hear any news. We don’t need to do more research on whether it makes sense to inform them. They already are telling us that they want that.”

Getz says most patients are not asking for extensive details about a drug. What volunteers want shortly after their trial has ended is a note saying that their participation was useful and that they will be sent information as results become publicly available.

“There’s been all this attention paid to filling trials but not on nurturing and reinforcing our appreciation for the people who have already been in our trials,” he said. “That is one of the new places where sponsors need to focus some energy and investment.”

Eli Lilly and Co. is one pharmaceutical company currently wrestling with how to publicly release results of clinical trials. It has established a Web site, Lillytrials.com, and in late 2005 pledged to post the results of all phase II–IV clinical trials within 1 year of trial completion or “as soon as possible” if there are significant safety concerns on any open trials. The company does not communicate results directly to patients who participate in trials but rather focuses on improving communication with participating physicians, said Jim Kremidas, manager of global enrollment optimization at Lilly. Communicating directly with patients is problematic for trial sponsors because of perceived conflict of interest, he said.

“The challenge is being able to [communicate results] while maintaining the patient’s privacy and the doctor–patient relationship,” Kremidas said. The question is “what can sponsors do maybe to get information back to the physicians more rapidly and how can we help the physicians have that conversation with the patients? At this point we’ve been focused primarily on communication with the physician. As for the next piece of the puzzle, I can tell you we don’t really have an answer for it right now.”

Patient advocate Mary Lou Smith, cofounder of the Research Advocacy Network and a breast cancer survivor, said physicians often want to share results, but the devil is in the details. Smith, currently cochair of the Eastern Cancer Cooperative Group’s Patient Representative Committee, said ECOG’s leadership voted to provide trial results to patients, but in practice roadblocks abound. Patients move or die. And often, hearing results can dredge up memories of a time they’d rather forget since many years often elapse between trial participation and results’ becoming available, she said. But despite these roadblocks, Smith says it is worth the time to create a system to share clinical trial results.

“I think that it is realistic to have a process in place that will allow participants, if they so desire, to view the results,” she said.

Kass said she believes the clinical research enterprise is entering a new phase in examining its responsibility to clinical trial participants. “There were some researchers who were kicking and screaming about the huge delays [informed consent] would impose on their research. ... But sometimes you have to do things, not because they are the most efficient, but because they are right,” she said.

© Oxford University Press 2007. DOI: 10.1093/jnci/djk039