Researchers Facing Increasing Costs for Clinical Research, With Few Solutions

Clinical and investigational tools of the 21st century have given cancer researchers the ability to target the disease in new, innovative ways. However, these great advances come at a time when costs are rising in essentially every area of running clinical trials, leaving cancer experts wondering who will pay for trials in the future. Cost increases can affect virtually every aspect of a treatment trial, but evaluating trial costs can be difficult.

Costs for any clinical trial depend on the number of patients, the type of trial, and the support systems needed. Phase I trials tend to be the most expensive and can cost $10,000–$15,000 per patient, in part because documentation requirements for each patient in early-phase trials can mean that reports reach 2,000 pages, said John Nemunaitis, M.D., oncologist and head of the Mary Crowley Medical Research Center at Baylor Health Care System in Dallas. Even in phase III trials, costs can run $5,000–$10,000 per patient. Physicians that head academic clinical cancer programs say that trial costs are increasing, in part, because hospital costs are on the rise, as are salaries for nurses and support staff. But pinpointing cost increases gets tricky.

“No one is tracking costs related to trials, and few places are trying,” said Neal Cohen, M.D., professor of anesthesiology and medicine and vice dean for the School of Medicine at the University of California, San Francisco. “In oncology, [tracking costs] is difficult because cancer treatments are protocol based, and in some cases we don’t have a single therapeutic intervention that is definitive.”

Cancer treatment comes as either standard-of-care or through a trial protocol. Cohen said that most National Cancer Institute–designated cancer centers have multiple, ongoing trial protocols, which makes it difficult for an institution to differentiate costs for routine care from protocol costs. If a patient receives standard therapy that calls for a follow-up computed tomography (CT) scan every 6 months and then that patient switches to a protocol requiring a CT scan every 6 months, is this a protocol cost or a routine cost? Will the insurance company or Medicare pay or not? The same question holds for all components of care, such as laboratory tests and office visits. “These are very difficult issues to address,” said Cohen.

Price of Committees

Many expenses critical to running a trial are not related to patient care but are for funding support staff and infrastructure. The Johns Hopkins Kimmel Cancer Center has not tracked the changes in costs of clinical trials, but their total cost of business escalates every year, and the support needed from the cancer center to fund infrastructure for trials gets higher and higher, said Ian Flinn, M.D., oncologist and the center’s associate director. For example, today’s regulatory climate requires that cancer centers provide separate, formal committees for safety and monitoring and for higher levels of internal auditing. Also, the number of patients that one nurse or data manager can handle annually is probably half of what it was 5 or 6 years ago, said Flinn.

The number of support staff needed continues to grow. The center now has auditors on staff, and they hired a Ph.D.-level scientist to support investigators in their effort to acquire investigational new drugs (INDs). They also have a GMP (good manufacturing practice) facility with its own staff for quality assurance as well as a research pharmacy with four pharmacists, who spend most of their time filling out paperwork to ensure compliance with regulations, he said.

“At the same time, funding has not gotten better,” Flinn said. “The clinical investigator is getting squeezed at both ends, and it’s difficult to be productive.”

Investigators at the center fund trials through a complex array of sources, said Flinn. Although researchers can apply for pilot funding provided by the center, they also fund their work through commercial sources, federal grants, or advocacy organizations. But the investigator does not pay for oversight, monitoring, and auditing, leaving those costs to the institution. “The cancer center is left with most of the ever-increasing oversight burden, including scientific review, auditing, and monitoring,” Flinn said. The cancer center funds these costs through a variety of sources as well, he said. Although philanthropy remains a critical source of funding for cancer research at many academic institutions, “no one wants to pay for infrastructure. They want to cure cancer, but they don’t want to pay for the committees,” Flinn said.

Institutional review boards (IRBs) also take a piece of the research funding pie. A letter to the editor in last April’s New England Journal of Medicine raised the concern that IRBs may not have the financial support to function well. The authors surveyed 121 academic institutions with active IRBs for 2002. Researchers broke down the costs of running these boards in the 63 institutions that responded, analyzing many factors including staff salary, board salary, space, training, monitoring, and compliance with federal regulations, such as the Health Insurance Portability and Accountability Act (HIPAA). Costs for HIPAA compliance in just the IRBs ran at 7% of total IRB costs.

“There’s no such thing as free legislation,” remarked lead author Jeremy
Sugarman, M.D., the Harvey M. Meyerhoff Professor of Bioethics and Medicine at Johns Hopkins University. He said that even though IRBs represent a small percentage of the costs needed to run a clinical trial, it is a cost that needs to be accounted for, and any assessment of what a clinical trial costs would need to undergo similarly rigorous accounting analysis.

More Early Studies

Cancer clinical trials are growing more expensive to run in part because researchers are collecting more information in phase I trials to determine early on whether a particular drug is worth pursuing, said Maurie Markman, M.D., vice president of clinical research at the University of Texas M. D. Anderson Cancer Center in Houston. For example, as scientists learn that lung cancer could be many different diseases, future treatments will need to reflect those diseases, he said. Traditionally, phase I trials assess treatment safety, but at M. D. Anderson, many early trials now also help characterize certain tumors. That means using sophisticated positron-emission tomography (PET) scans with experimental isotopes. In turn, these imaging data need to be followed by more blood tests and molecular analysis of tissue to correlate results—work, Markman said, that is not covered by basic research grants.

At Baylor, Nemunaitis is working on the type of targeted research that builds on genomic and proteomic discoveries—the type of targeted therapies, Nemunaitis said, that large pharmaceutical companies are reluctant to fund. He and his colleagues have already started a study to identify a small set of genes that are activated only in each patient’s cancer cells but not in healthy ones. They will use this genetic profile to identify the genes and then match the patient to the best U.S. Food and Drug Administration–approved therapeutic.

These targeted therapies require comprehensive assessment of patients enrolled in the trials, which bumps up costs because these trials require more support personnel and intense nursing time. They also require extra radiographic monitoring with CT and PET scans, which represents their greatest costs, he said.

Who Really Pays?

Although institutions such as the Kimmel Cancer Center are adapting to the high cost of clinical trials, Flinn expressed concern about what future cost increases could mean for cancer research in the long term. “It will deplete the number of clinical investigators because it’s getting very difficult to do this kind of work and very discouraging,” he said. If clinician–scientists need to look for industry sponsors for their clinical trials, that has ramifications as well because industry will exert a greater influence on the way research is conducted, Flinn said.

But even when clinical researchers seek pharmaceutical sponsorship, they can find support difficult to secure. If a company has a promising drug to treat
lung cancer but an academic researcher wants to test that drug for a rare leukemia, the company may fund only data management and ask the institution to pay for imaging and patient monitoring and to hold the IND, Markman said.

“The issue with an institution holding the IND relates to the tremendous regulatory requirements associated with this process. Therefore, it is not only a question of costs but of the experienced personnel required to provide FDA-mandated oversight of such studies. If the institution holds the IND, this becomes their responsibility, not [that of] the pharmaceutical company,” said Markman.

The problem, he said, is that there are no “bad guys,” just the combination of many factors with no simple solutions. But if money cannot be secured to fund the extra costs, clinical investigation could be in jeopardy, Markman said.

Reducing the burden of cancer will take more than money, although extra money would help, said Markman. He would like to see the FDA, the Office for Human Research Protections, and the NCI simplify and coordinate rules to build efficiencies into the system without compromising safety. Reducing costs could help ensure that no promising therapy is left behind.

He also suggested federal legislation requiring 1% of premiums paid to insurance companies be pooled into a fund and allocated to research of merit. This funding would be independent of, for example, NCI investigator–initiated studies. Even a 0.5% tax on premiums would be helpful. “That would take tremendous political will,” Markman said.

Nemunaitis said the financial side is something he does not think he can influence. “I have so many things to focus our worries on. I’m probably more of a blue-collar worker. I’m worried more about my patients today and if they are getting the best treatment, and how we can make the individualized approach come into reality sooner,” he said. “Everyone knows this is the way it’s going to be in the future, but sometimes knowing what is going to be and making it happen today are two different things, and they shouldn’t be.”

—Jeanne Erdmann