CLINICAL RESEARCH: WHO PAYS THE BILL?

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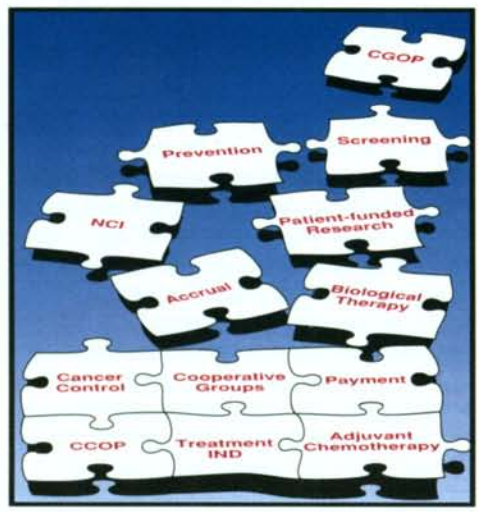
Has the time come for patient-funded clinical research? This article describes the establishment of clinical research in the private sector, how it is funded, and how that funding compares with research conducted in the public sector.

Historically, clinical research has been conducted primarily by government and university institutions. Money has been available for the conduct of clinical research through government grants and philanthropy, as well as drug company profits. As these public research efforts have broadened, this funding base has provided less of the total cost, and insurance companies and patients have come to pay for the greater portion of clinical research.[1-3]

For instance, in the early 1980s, insurance companies were billed for the cost of patients' clinical care in one of the earliest Phase I and, later, Phase II trials of alpha Interferon, which were administered through the Biological Response Modifiers Program (BRMP) at the National Cancer Institute (NCI). The alpha Interferon was supplied by Hoffmann-La Roche (Roferon) after the gene was cloned by Genentech. Physicians and clinical facilities were made available at Frederick Memorial Hospital under the aegis of the NCI. The clinical costs were paid by the patients' insurers, and the NCI covered costs not reimbursed by third-party payers. This arrangement, and the insurance funding of Phase II and Phase III clinical trials conducted by NCI clinical cooperative groups in the university system, made it clear that clinical research was, and still is, predominantly funded by insurers and, ultimately, the employers and patients who pay the insurance premiums. Philanthropy, government grants, and the profits of pharmaceutical houses often contribute by paying investigator and nurse salaries and laboratory ancillary costs. However, the greatest expense of clinical research, hospital care, is primarily reimbursed by the patient's insurance company.



Recognizing these facts, Biotherapeutics, an investor-owned, for-profit company, was established in 1984 to make available certain laboratory services necessary for the delivery of selected forms of cancer biotherapy. It became obvious in the mid-1980s, that monoclonal antibody technology, lymphokine/cytokine applications, and lymphocyte expansion required laboratory technologies for their generation and testing and often were needed to produce sufficient amounts of the materials in a specified way for the clinical research program. The use of the laboratory in clinical medicine was the basis for Biotherapeutics' concept that selected forms of cancer biotherapy would not come simply to the pharmacy as a pill or an injection, but would require laboratory enhancement and monitoring.

Because laboratory procedures, in the absence of clinical application, simply represent basic research, an independent organization, the Biological Therapy Institute (BTI), was established in 1984 for the conduct of clinical research. BTI, a nonprofit, tax-exempt organization, conducts clinical research and educates oncology professionals through its clinical trials group, the National Biotherapy Study Group (NBSG) and NBSG's system of affiliated hospitals.

Currently, NBSG protocols are available at more than 20 metropolitan hospitals across the United States and as far west as Hong Kong. NBSG investigators must be certified through the BTI/NBSG education course to use NBSG protocols. The credentialed, practicing oncologists at these hospitals must be registered with the FDA to participate as NBSG investigators. All of the NBSG protocols are focused on cancer biotherapy (although some of the studies have interdigitated chemotherapy or radiotherapy treatments), and receive both extensive internal NBSG review and external FDA review. Currently, these protocols are in the process of being listed on the NCI's PDQ system. The rapid growth in this private sector clinical research program (see the table on next page) demonstrates the desire of oncologists in private practice to provide experi-

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Growth of the National Biotherapy Study Group 1988-1989

	January 1988	January 1989
Clinical Sites	12	22
Membership	34	125
Protocols	10	17
Biologics in Use	3	6
Biopharmaceutical Sources	2	4
Cumulative Patient Accrual	248	555

mental options to their patients.

The laboratory analyses and enhancements required in the NBSG clinical protocols are delivered through the hospital laboratory when such services are available or, if necessary, through a Biotherapeutics laboratory. Therefore, the clinical research system operates through a series of largely non-profit hospitals, and conducts clinical research in the usual manner, using support services from other organizations as needed.

Since the inception of Biotherapeutics, BTI, and the NBSG, we have recognized that the cost of clinical research is a major factor in whether or not new technologies are applied in the practice of oncology. In understanding that clinical research patient care costs have predominantly been funded by insurers, employers, and patients, we chose to expand on the government/university system and allow the technology to be dispersed in the private sector, rather than requiring the patient to travel to a regional cancer center. The concept behind the NBSG clinical research program is very similar to the NCI's Community Clinical Oncology Program (CCOP) in that it makes the protocols (and, in the case of Biotherapeutics, some of the rather intensive laboratory capabilities) available at the metropolitan and community hospital level. NBSG protocols require the usual Institutional Review Board (IRB) approval, and obviously, where investigational products are concerned, review and registration with the FDA and the product manufacturer. Thus, the conduct of these clinical trials is no different from that of CCOP protocols with the exception that 1) NBSG protocols have broader eligibility criteria, 2) the studies are somewhat more individualized, and 3) the protocols concentrate on cancer biotherapy in contrast to the current CCOP emphasis on chemotherapy.

Insurers are billed for the clinical services associated with NBSG patients, much as they are for the patients enrolled on CCOP and university studies. However, when insurers have been unwilling to pay clinical and laboratory costs, patients have directly borne some of the costs of those services. Thus, the concept of direct, patient-funded research was conceived.[3] In reality, most clinical research is patient-funded, the difference being that the research is funded through the patients' or their employers' contributions to insurance premiums, as opposed to direct payment for services.

What are the problems and opportunities of clinical research in the private sector? They are very similar to the problems and opportunities of clinical research in the public sector. In the absence of taxpayer funds or pharmaceutical company profits to support the clinical research, someone must pay. In both systems, the insurer and employer play increasingly important roles in the determination of who has access to, and who pays for, clinical research. Clearly, consensus is needed to determine what level of clinical research services should be provided to patients with cancer and other life-threatening diseases. An agreement needs to be reached among government, insurers, hospitals, physicians and patients as to what is a reasonable and equitable system of using patients' insurance premiums for medical care. This issue has not been properly addressed and currently represents the greatest impediment to effectively translating new technology developed through clinical research into standard treatment.[4,5] A second barrier is the Food & Drug Administration (FDA). The FDA has the capability of liberalizing regulatory guidelines to make new products, most specifically new products of the biotechnology industry, available more rapidly through the clinical research paradigm.[6]

Much of oncology care today involves the delivery of approved, but relatively ineffective drugs, for the treatment of advanced cancer. Today, more than 50 percent of the one million patients who will develop cancer in the United States will die of their disease. Most of these patients will receive approved drugs and be reimbursed for their care, but their disease will not be effectively treated. The time has come to recognize clinical research as the opportunity for such patients. To that end, we need to increase the availability of clinical research products and protocols under an adequate system of reimbursement.

Perhaps a managed care concept, where a sum of money is made available through third-party payers by diagnosis-related group (DRG), would increase opportunities for the patient. The patient, in concert with the physician and the medical care team, could then participate in the decisionmaking process of whether or not to try standard treatment or experimental treatment. As long as the costs are capped and agreed upon, insurers won't be at increased risk of rising health care costs, and patients will be afforded the option of substituting clinical research for standard treatment.

Private sector cancer research and treatment are here to stay. They are impacting the publicly funded research system by complementing and broadening it. Eighty percent of patients with cancer are treated in the private sector. Approximately 50 percent of patients entered on NCI protocols are enrolled through the CCOP's private sector system. Moreover, less than five percent of cancer patients currently enter public sector research protocols, while 30 percent or more might be eligible. Therefore, it is important to recognize that clinical research and clinical care are indelibly linked and most efficiently delivered in the private sector by qualified oncologists at credentialed hospitals that are located near the patients, their families, and their support systems. Such has been the design of the federally funded CCOP program. In a similar manner, the Biological Therapy Institute, through the National Biotherapy Study Group's clinical research program in the private sector, and Biotherapeutics have endeavored to deliver clinical and laboratory services to physicians and hospitals in the community setting. More clinical research should be encouraged in the private sector with all parties (hospitals, insurers, pharmaceutical companies, physicians, patients and employers) agreeing to pay their fair share of the costs.[7] ■

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