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The National Surgical Adjuvant Breast and Bowel Project

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can be readily transferred to the community setting. Because of the complex nature of these trials, it is important that community physicians be capable of providing identical treatment programs that duplicate previous successes. Obviously, cancer treatments that cannot be administered by community physicians greatly reduce the number of future patients that can be cured and compromise cooperative groups' efforts to increase cancer survival.

The Southwest Oncology Group CGOP participants are fully involved in all new group scientific initiatives. Outreach investigators have been included in group trials using investigational new agents and in basic science studies requiring contributions of specimens. These ancillary biologic trials include several leukemia biology studies (French-American-British Classification System for Leukemia, cytogenetics, flow cytometry, and proto-oncogene expression); flow cytometry in genitourinary cancer, breast cancer, head and neck cancer, sarcoma, and lymphoma; and pharmacokinetics studies in gynecological cancer, as well as lymphoma and myeloma immunophenotyping. Cancer control studies (i.e., quality of life studies in brain, breast, and genitourinary cancer patients, smoking cessation in bladder cancer patients, and evaluation of reproductive function in testicular cancer patients) are also open to CGOP investigators. Contributions are provided by the CGOP affiliates to rapidly address and answer these complex and important research questions.

The CGOP membership has assumed an active role in the group's largest cancer prevention study, the Prostate Cancer Prevention Trial, launched nationwide in October 1993. This study is the first large-scale prevention trial for prostate cancer and will enroll 18,000 men age 55 and older in a seven-year double-blind study to test whether taking the drug finasteride will prevent prostate cancer. The Southwest Oncology Group is coordinating this intergroup study, which includes participation by the Eastern Cooperative Oncology Group, the Cancer and Acute Leukemia Group B, Community Clinical Oncology Program affiliates, and NCI-supported cancer centers. Twenty-three of the participating 227 sites are CGOP affiliates; as of March 16, 1994, they have been responsible for enrollment of 991 of the 10,296 men accrued to the study.

Although significant strides have already been made toward the integration of community practitioners in cooperative group research, there still lies potential for even greater participation in successful cancer research. The future success of outreach programs is contingent on the commitment of the National Cancer Institute, each cooperative group, and the community physicians themselves. Problems in the community setting must be identified and the solutions implemented if we are to guarantee major reductions in the national cancer mortality rate.

The National Surgical Adjuvant Breast and Bowel Project

by Bernard Fisher, M.D., Arthur P. DeCillis, M.D., D.L. Wickerham, M.D., and Walter M. Cronin, M.P.H.

The National Surgical Adjuvant Breast and Bowel Project (NSABP) is a multidisciplinary cooperative group that conducts clinical trials in breast and colorectal cancer. Since its inception in 1958, the NSABP, under the leadership of Dr. Bernard Fisher, has played an important role in improving the treatment and management of these cancers.

In an earlier article in *Oncology Issues* (Vol. 4, 1989) Dr. Fisher and Mr. Cronin stated the belief that clinical trials can flourish only if community-based physicians are involved and invested in this research. In the early 1970s, the NSABP took the initiative to increase the participation of community-based oncologists in clinical studies. This effort provided the model for the National Cancer Institute's establishment of the Cooperative Group Outreach Program (CGOP) and the Community Clinical Oncology Program (CCOP). The results of these efforts are apparent. Since 1988, community-based institutions have entered more patients on NSABP studies than university or NCI-designated cancer centers (Table 1). Today, the majority of NSABP institutions are not affiliated with university-based medical centers. Community-based physicians participating in our studies are primary contributors to the improvement of breast and colorectal cancer treatment. This is very appropriate since clinical oncologists are also primary consumers of the results of clinical studies and, according to clinical research findings, make scientifically justified therapeutic decisions. Hence, we are committed to expanding the involvement of community-based investigators and including their diverse patient populations in NSABP clinical trials.

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CHANGING THE PARADIGMS

The NSABP has always been committed to conducting clinical research that changes the paradigms of cancer management. Under Dr. Fisher's direction, the NSABP's past trials in breast cancer have resulted in the change of standard surgical treatment from mastectomy to lumpectomy, the shifting of chemotherapy to the adjuvant setting, and the widespread use of tamoxifen in postmenopausal women, particularly those with high estrogen-receptor values.

Recently, the NSABP demonstrated the importance of radiation therapy to lumpectomy in patients with noninvasive ductal carcinoma. We have implemented and completed breast cancer trials evaluating the impact of preoperative chemotherapy, as well as the value of administering intensified and increasing amounts of chemotherapy with colony-stimulating factor support. Our studies have tested the impact of 5-FU modulation on colon cancer outcome.

The NSABP has continued to expand the scope of the hypotheses to be tested in breast and colorectal cancer studies. In 1992 we began the Breast Cancer Prevention Trial to test whether long-term tamoxifen therapy is effective in preventing the occurrence of and mortality due to invasive breast cancer. With the goal

of accruing 16,000 women, approximately 8,000 women entered the study in the first year. This study has the additional objectives of evaluating the expected benefit of tamoxifen on cardiovascular mortality and the incidence of bone fractures, as well as evaluating the risk-benefit ratios of tamoxifen prevention therapy.

In other breast cancer trials, we are departing from the conventional wisdom of treating all node-negative women equally. Our new protocols will use markers to assess a woman's risk of breast cancer recurrence and test appropriate therapies based on that risk. We will continue our evaluation of preoperative chemotherapy and the impact of the primary tumor response on outcome. We are also venturing into a clinical trial with a geriatric population. Despite representing a significant proportion of breast cancer patients, remarkably little reliable clinical data exists to guide physicians in the management of these patients.

One of the NSABP's most challenging trials is to evaluate the worth of preoperative multimodal therapy in patients with operable rectal cancer. In addition to evaluating the effect of preoperative therapy on survival, and disease-free survival, this study will assess whether patients can be converted to sphincter-saving surgical procedures by shrinkage of the primary tumor.

This description of our ongoing trials is evidence that the NSABP does not shy away from complex protocols if they have the potential to answer a clinically important question. Likewise, the community investigators have not been intimidated by the increasing complexity of some of our trials. The percentage of patients that community-based physicians enter onto NSABP protocols is consistently larger than university-based investigators, irrespective of the stage of the disease.

COMPLIANCE AND MOTIVATION

Entering patients onto a study is only one aspect of clinical research. Vital to the success of a study is compliance with protocol requirements. These requirements include 1) providing documentation of eligibility, 2) submitting data on patient adherence to therapy and follow-up testing, and 3) monitoring adverse drug reactions. By all criteria, community investigators have demonstrated their ability to successfully participate in clinical studies. In order to ensure a continuation of the distinguished research that the NSABP has performed, both community- and university-based NSABP investigators must also demonstrate the commitment to adhere to the highest standard of scientific conduct. The NSABP headquarters and membership are committed to the science of clinical trials and improvements in clinical practice through clinical research.

An important issue regarding community-based investigators is that they participate largely on a

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Table 1. NSABP accrual 1988–93

Comparison of accrual rates to NSABP protocols between university and cancer centers and community-based centers from 1988 to 1993.

Year	University & Cancer Centers	Community-Based Centers	Total
1988	1,619 (42.7%)	2,175 (57.3%)	3,794
1989	1,329 (38.6%)	2,109 (61.3%)	3,438
1990	1,843 (37.4%)	3,090 (62.6%)	4,933
1991	1,004 (46.5%)	1,156 (53.5%)	2,160
1992	1,534 (40.0%)	2,296 (60.0%)	3,830
1993 (Jan.-Sept.)	1,023 (34.8%)	1,916 (65.2%)	2,939
Total	8,352 (39.6%)	12,742 (60.4%)	21,094

Research in the Multispecialty Clinic

by Richard N. Re, M.D.

As the year 2000 approaches, researchers are making daily extraordinary advances in molecular genetics and in the understanding of pathogenesis of human disease. In the area of health care delivery, integrated models and physician group consolidation are increasing, and novel payment schemes are proliferating. At the same time, the government is proposing major health care reform. But because the specifics of this initiative are unknown, considerable uncertainty remains as to the form the health care system will assume.

Against this backdrop of frenzied activity, the physician, scientist, or administrator may wonder what place, if any, research has in the multispecialty clinic. This question becomes all the more poignant as margins from health care delivery fall, resulting in the decline of expendable income for research activities. At the same time, the National Institutes of Health and other federal funding agencies are finding it increasingly difficult to support a growing number of proposals for research activities. Indeed, it could be argued that research activities are a luxury the multispecialty clinic can no longer afford. This view, however, is incorrect.

THE BENEFITS OF RESEARCH

Now, more than ever, research forms an integral part of quality medical care, a view based on the fact that two major paradigm shifts are occurring simultaneously in the medical world. The first of these is the shift from physiology-based medicine to genetics-based medicine; and the second is the supplementation of clinical judgment with health services research. The first of these

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