THE CANCER LETTER

Vol. 20 No. 19
May 13, 1994

Price $225 Per Year US, Canada
$250 Per Year Elsewhere

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

NCI Considers Taking Prevention Trial From NSABP; Other Groups Approached

NCI is considering removing the Breast Cancer Prevention Trial from the cooperative group that three years ago won the $60 million grant to conduct the trial, **The Cancer Letter** has learned this week.

NCI officials confirmed that the Institute is reviewing two options: transferring the trial from the National Surgical Adjuvant Breast & Bowel Project to another cooperative group, or hiring a contractor to manage the trial.

"We are exploring all of the options open to us to get the trial running again as quickly as possible, while maintaining the confidence of the women on the trial and the safety of the trial," Leslie Ford, acting deputy director

(Continued to page 2)

In Brief

Connell Is President Of Komen Foundation; Ravikumar Moves To New Jersey Cancer Inst.

NANCY CONNELL has been appointed president of the Susan G. Komen Breast Cancer Foundation, the foundation's Board of Trustees announced. Since 1990, Connell has served as executive director of the Northeast Texas chapter of the Cystic Fibrosis Foundation. Prior to that position, she was director of education for the Young President's Organization. . . . **T.S. RAVIKUMAR** was recently named associate director and chief of surgical oncology at the Cancer Institute of New Jersey. Ravikumar, former director of surgical oncology and co-director of the Comprehensive Breast Center at Yale, also was appointed professor of surgery and molecular biology at Robert Wood Johnson Medical School. . . . **CLIFTON POODRY** has been named the first director of the Minority Opportunities in Research Programs Branch of the National Institute of General Medical Sciences. Poodry joins NIH from the Univ. of California, Santa Cruz, where he has been professor of biology since 1983. . . . **ONCOLOGY NURSING** Foundation established the Marion Merrell Dow Inc. Research Fellowship Award to support short-term oncology-specific research training for Oncology Nursing Society members who lack access either to a graduate level curriculum in oncology nursing or to a senior oncology nurse researcher. Maximum of $10,000 will be awarded. Application deadline is June 1. Contact ONS Research Dept., Tel. 412/921-7373. . . . **HAHNEMANN UNIV.** has won a four-year, $960,000 grant from NCI to study a problem-solving approach to helping persons with cancer improve their quality of life. Principal investigator of the study is **Arthur Nezu**.

NSABP Surprised To Learn Of Talks On Prevention Trial

(Continued from page 1)
of the NCI Div. of Cancer Prevention and Control, said to **The Cancer Letter**.

The prevention trial was halted six weeks ago, along with all NSABP trials, after NCI discovered that the cooperative group's audits of its member institutions were behind schedule. NCI officials and other scientists say the trial may have the greatest potential of all the NSABP's current studies to alter the standard of care for the prevention of breast cancer.

NSABP has submitted a reorganization plan to NCI that includes improved auditing and monitoring of clinical trials. However, NCI may not be willing to wait for the plan to be put in effect. Moreover, any plan that includes resuming the prevention trial may require more personnel than NSABP has available, sources in other cooperative groups said to **The Cancer Letter**.

"The whole confidence in the trial has been shaken," one investigator said. "Anyone who takes it over will have to audit all the trial's data." An extensive audit that would examine a random sample of participant data from each of the 270 prevention trial sites would cost at least $1 million, the investigator said.

The Cancer Letter has learned that NCI has held discussions with the Southwest Oncology Group about taking over the prevention trial, though no definite plans for a transfer have been made. SWOG officials confirmed that discussions had taken place. "Dr. Broder has spoken to many individuals on ways to salvage the prevention trial, including the Southwest Oncology Group," SWOG executive officer Mace Rothenberg said to **The Cancer Letter**.

THE CANCER LETTER

Editors: **Kirsten Boyd Goldberg**
Paul Goldberg
Founder & Contributing Editor: **Jerry D. Boyd**

P.O. Box 15189, Washington, D.C. 20003
Tel. (202) 543-7665 Fax: (202) 543-6879

Subscription $225 per year North America, $250 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter.

'Surprised And Shocked'

In a recent letter to NCI Director Samuel Broder, NSABP interim principal investigator Ronald Herberman wrote that he had heard rumors about NCI's plans and urged the Institute to reconsider.

"I am surprised and, in fact, shocked to learn this...when I and [interim executive officer Donald] Skip Trump have been acting in good faith and with virtually complete dedication of our time and energies to stablize the NSABP and to correct all of the administrative and procedural problems," Herberman wrote in a letter dated May 9. "I urge you to reconsider your plans and to allow us to demonstrate to you that the NSABP, under its new leadership, is fully capable of completing the BCPT."

At last week's meetings that involved Trump, Ford, and DCPC advisory groups, "no hint of this consideration was given, and all feed-back about what we are doing was positive," Herberman wrote.

A copy of Herberman's letter was obtained by **The Cancer Letter**.

Ford said no decision has been made to change the management of the trial. "We are indebted to Dr. Herberman for all he has done, but we do have to explore all the options," she said. "Dr. Broder made it clear last week that our first priority is reopening the prevention study and restoring the confidence of the people on the trial."

The purpose of the meetings with the cooperative group last week was to discuss the scientific issues surrounding the trial, including the risk of endometrial cancer from tamoxifen, Ford said.

The group's ability to audit the research sites is NCI's primary concern, Ford said. "In a study this big we want to be sure that we have no shadows over us," she said.

For investigators and participants, removing the study from NSABP would be "a matter of changing the address where they send things," Ford said. "Sites would remain the same and people working on the study will continue to be employed."

'Incomplete Records' Cited

The NSABP Executive Committee passed a resolution opposing a move of the prevention trial, Herberman said in an interview with **The Cancer Letter** this week.

"At this critical time in the hisotry of the NSABP, this removal of an important trial might contribute to the dissolution of the group," Herberman said. Members of the NSABP Executive Committee have said that if the prevention trial is removed, they would consider ending their participation in the trial.

Herberman said that in a "long discussion" following Broder's receipt of the letter, the NCI Director said the Institute was concerned about the group's administrative and reporting problems.

"He mentioned auditing of the prevention sites over the last several months, which have indicated a rather high percentage of incompete records," Herberman said. "We feel this is largely a reflection of the difference between a prevention trial and a more traditional treatment trial, and a much greater likelihood that many of the needed records would not be present at the site where the prevention trial is being conducted."

In many cases, the records of the physical exams and original participant entry data were not kept at the prevention trial sites, he said.

"We have taken steps to ensure new processes so that these records from now on will be available at the sites where the audits are taking place," Herberman said. "We do not believe that this reflects fundamental problems in the eligibility of the participants.

In his letter to Broder, Herberman outlined his arguments for keeping the trial in NSABP:

- The need for continuity. Community oncologists involved in the study are "strongly loyal to the NSABP and there is a strong possibility that a shift away from the NSABP, on top of the loss of Dr. [Bernard] Fisher as the leader, will lead to many dropping out of participation and jeopardizing the continuity of drug administration and follow-up."
- "The need to maintain the confidence of the women who are participating in the trial.... The break in continuity, in additon to the concerns that have been raised about the risks of tamoxifen, is likely to undermine confidence in the trial and NCI's ability to lead it."
- "The plan for corrective action that the NSABP has been developing will provide the solution to the problems of the past, and it is therefore entirely unnecessary to make a further, drastic move. The Oversight Committee, including both experts in clinical trials and breast cancer advocates, are fully supportive of this plan and have given us confidence in its effectiveness."
- "We have directly recognized the need for more attention to the risk of endometrial cancer and are far along in developing a feasible plan for regular, mandatory endometrial sampling of all participants on both the prevention and treatment trials."
- "I believe the central basis for your concern, i.e., the performance of Dr. Fisher in regard to the risks associated with tamoxifen, has already been dealt with and there is no need to further disrupt the NSABP."

Nearly 11,000 women are enrolled in the prevention trial, and 5,000 more are needed to complete accrual.

NCI Advisors: Resume Trial, Add Endometrial Sampling

The Breast Cancer Prevention Trial, halted by NCI last month, should be modified and resumed as soon as possible, an advisory board said last week.

Advisors to NCI's Div. of Cancer Prevention & Control voted unanimously to recommend the resumption of the study, which is testing tamoxifen for the prevention of breast cancer in healthy women at increased risk of the disease.

Patient accrual to the $60 million, 10-year prevention study was halted April 4 in a suspension of all trials by the National Surgical Adjuvant Breast and Bowel Project, which followed NCI's discovery that the cooperative group was behind schedule in auditing its research sites.

As one condition of resuming accrual, NCI said the cooperative group must develop a functional audit program. The trial involves 270 research sites.

The suspension of the prevention trial also followed NSABP's publication of data in a previous study of the risks associated with long-term tamoxifen use, including the risk of death from endometrial cancer.

Annual Endometrial Sampling Advised

Endorsing a recommendation from the prevention trial's safety monitoring committee, the DCPC Board of Scientific Counselors said accrual to the trial should resume if the following conditions are met:

- Participants should be fully informed about the risks and benefits of taking tamoxifen in regard to their own personal circumstances, particularly with regard to age.

• Annual endometrial aspirations should be done for participants who have not had a hysterectomy.

• There should be no change in the eligibility requirements.

Theodore Colton, chairman of the prevention trial's Endpoint Review, Safety Monitoring, and Advisory Committee (ERSMAC) told the NCI advisors that the committee reviewed the cumulative unblinded data and found there was no reason to stop the trial due to toxicity or efficacy.

The safety monitoring committee also adopted a provision that if there is an imbalance in the number of endometrial cancer cases on either arm of the study, the committee would be alerted to look further at the unblinded data.

If the annual endometrial aspirations are instituted and participants are fully informed, the trial should resume as soon as possible, Colton said.

Trial Not Without Controversy

"This trial has not been without controversy since its very inception," Leslie Ford, chief of DCPC's Community Oncology & Rehabilitation Branch, said to the board. The branch oversees the prevention trial.

The trial began in April 1992, and requires 16,000 participants who are randomized to receive either tamoxifen or a placebo for five years.

In addition to preventing breast cancer, tamoxifen also is believed to reduce the incidence of cardiovascular events and bone fractures. Add-on studies to the trial are examining participants for endometrial changes, bone and mineral metabolism, and genetics. Another study is looking at the effect of tamoxifen on the participants' quality of life.

A woman is eligible for the prevention trial if her risk of contracting breast cancer in the next five years is equivalent to that of the average 60-year-old.

As of the end of March, NSABP had performed nearly 66,500 risk assessments, finding 11,369 women eligible for the study, and randomizing 10,883 women, Ford said.

About 40 percent of the participants are age 35-49; about 30 percent are age 50-59; and 30 percent are age 60 or over.

Participants in the study tend to be at much higher risk of breast cancer than is required for enrollment, Ford said. For example:

• At every age group except the youngest, the average relative risk for breast cancer of the participants is nearly twice the risk required for entry, Ford said. About 40 percent of the participants have a relative risk of 10.01 or more, and more than 30 percent have a relative risk between 5 to 10. The required risk is 1.7.

• About 80 percent of all participants under age 50 have at least one first-degree relative with breast cancer.

• More than 40 percent of the women randomized have had lobular carcinoma in situ, making the prevention trial the largest study of this breast cancer risk factor.

"When we started this trial we knew there was an increased risk of endometrial cancer," Ford said to a May 4 meeting of the trial's working group. NCI did not require, and did not provide funds for endometrial sampling.

Last January, NCI notified investigators that women taking tamoxifen have a higher risk of contracting and possibly dying from endometrial cancer than women not taking the drug. Informed consent forms for the prevention trial were rewritten to remove a statement that no patient had died from endometrial cancer in previous trials of the drug (**The Cancer Letter**, April 29).

NSABP published a study of endometrial cancer cases in the B-14 study testing tamoxifen as treatment for breast cancer in the April 6 issue of the Journal of the National Cancer Institute.

According to the report, there were 25 cases of endometrial cancer in the B-14 study, and five deaths due to the disease. Four of the patients who died of endometrial cancer had been randomized to receive tamoxifen, but one patient never took the drug. There was one death from endometrial cancer in a group of patients registered on the trial, but not randomized.

Ford told the working group that in a third of the endometrial cancer cases, patients had received prior hormone therapy. In one case, Ford said, a patient had breast, then colon, and then endometrial cancer.

"We don't fully understand the histology of the endometrial cancer cases in B-14," Edward Trimble, an investigator in NCI's Div. of Cancer Treatment, said at the working group meeting. "It is unclear whether they are related to estrogen or whether tamoxifen has some unidentified carcinogenic effect."

Carolyn Runowicz, of the obstetrics and gynecology department at Montefiore Medical Center, said her "wish list" for the prevention trial would include a baseline endometrial sampling, and baseline and annual endometrial sonograms. "If we

add sonography now, we may end up preventing endometrial biopsies," she said.

Endometrial sampling is a condition of entering the study at Univ. of California, Los Angeles, said Patricia Ganz, chief of hematology/oncology. Morbidity of the procedure is low, she said. Women undergoing the procedure experience cramping, but most perceive it as temporary discomfort necessary to the study's safety.

About 35 percent of women in the trial have had hysterectomies, she said, and thus would not require the procedure.

Broder: Change Eligibility Requirement

NCI Director Samuel Broder asked the working group to consider increasing the breast cancer risk required for entry in the study.

"Women at exceedingly high risk have entered the study in large numbers at every age group, essentially voting with their feet," he said. "I can see certain benefits and little or no downside to changing the eligibility of the study.

"The solution to me is obvious that we need to change the eligibility," Broder said. "There is a natural resistance to changing a study in mid-stream."

William Harlan, director of the NIH Women's Health Initiative, said the downside to changing the eligibility would be more difficulty in recruitment.

Colton noted that breast cancer reduction is not the study's only endpoint. The prevention trial is jointly funded by the National Heart, Lung & Blood Institute, which is seeking data on tamoxifen's effect on reducing cardiovascular disease in women.

Such a change in eligibility could result in "negative publicity" that could affect the compliance of women taking tamoxifen in the study, said Lawrence Freedman, chief of DCPC's Biometry Branch.

"We are very concerned about the compliance in this trial," Freedman said.

Amy Langer, executive director of the National Alliance of Breast Cancer Organizations, noted that the Senate Cancer Coalition was scheduled to hold a hearing this week on the prevention trial. "Eligibility criteria is on their minds," she said. "Someone has to have a definitive answer or say that we are open to change."

Countered board member Charles Hennekens: "We are a board of scientific counselors, not a board of political counselors."

Victor Vogel, a prevention trial investigator from M.D. Anderson Cancer Center, said the prevention trial already has re-consented participants four times since the trial began. "There have been four separate revised informed consent documents and a 'Dear Participant' letter," he said. "The trial has exceeded the bounds of informing participants of the risks."

Board member David Alberts, a prevention trial investigator from Arizona Cancer Center, agreed. "We have to be more sensitive to the individual investigator," he said. He termed the participant letter "hysterical mail that we have been forced to send out."

At the Board of Scientific Counselors meeting the following day, board member Ian Thompson said the board's subcommittee on early detection and community oncology considered the question of raising the risk required for eligibility.

The subcommittee recommended against the change, Thompson said, because it would damage public perception of the study, which might lead to a decrease in compliance and a decrease in the statistical power of the study and it would delay the reinstitution of the protocol.

The subcommittee felt the eligibility issue was less important that the recommendation to conduct endometrial sampling, Thompson said. In addition, the final decision to participate is left to the individual, who would be adequately informed about the risks and benefits, he said.

NSABP statistician Joseph Constantino said that, based on the breast cancer risk of women enrolled in the trial, the prevention study is expected to prevent 132 breast cancers and 65 cardiovascular events. However, tamoxifen would be expected to cause 84 endometrial cancers, two liver cancers, and four deaths from pulmonary embolism.

That, Constantino said, still amounts to a net benefit, even if the actual cardiac benefit is only half what the study planners expected.

Fisher, Redmond Removed From Official Posts At NSABP

Bowing to an ultimatum from NCI, the Univ. of Pittsburgh has revised its proposal for restructuring of the National Surgical Adjuvant Breast & Bowel Project by withdrawing the appointment of Bernard Fisher to the post of scientific director.

In effect, the change will end Fisher's official role in the cooperative group. Carol Redmond, NSABP's

chief biostatistician, was also removed from formal dealings with the group, the university said.

Earlier this month, NCI threatened to withhold funding for NSABP until the group removed Fisher and Redmond from leadership positions. In a related action, the NIH Office of Research Integrity ordered the Univ. of Pittsburgh to start an investigation of possible scientific misconduct by the two scientists (**The Cancer Letter**, May 6).

"In the course of discussions with NCI, it has been agreed that Dr. Fisher will not hold a leadership position and will not have any time committed to the cooperative agreement that provides support to NSABP," Ronald Herberman, the cooperative group's interim principal investigator, said to **The Cancer Letter**.

"It has been agreed that Dr. Fisher can continue his research and can interact as a colleague with NSABP staff and investigators, and he will be available for consultation," Herberman said.

Both Fisher and Redmond will retain their teaching positions at the university. Herberman said an inquiry panel is being assembled by the university to investigate the charges of scientific misconduct against the two.

The inquiry panel, which is likely to include four experts with no affiliation to the university, will have until June 27 to determine whether a full investigation is warranted.

The panel will be asked to decide whether Fisher and Redmond had knowingly included fraudulent data from Roger Poisson, an investigator at St. Luc's Hospital in Montreal, in publications based on research by the cooperative group.

It is highly unusual for an institution to remove researchers from involvement in NIH-funded research prior to the start of a misconduct investigation, several observers said.

Pittsburgh Reprimands Staff For Use Of Univ. Resources

Several staff and faculty members of the Univ. of Pittsburgh were found to have used university equipment in preparation of an anonymous mailing to NSABP principal investigators.

The mailing urged cancer researchers to write letters to Congress and the Administration, demanding the reinstatement of Bernard Fisher to chairmanship of NSABP and an investigation of NCI's "unfair treatment of Dr. Fisher."

According to a university spokesman, letters of reprimand will be placed in the personnel files of staff and faculty members who played a role in preparing the mailing.

Jane Duffield, the spokesman, declined to reveal the names of the persons involved or to say how many employees were reprimanded.

"Letters of reprimand will be issued to the university employees involved," Duffield said to **The Cancer Letter**. "Consistent with the university policy, we will not reveal any names.

"The university auditors believed that there was a concerted effort made to separate this activity from university business, even though there was a small use of the university equipment and the UPS rate."

The letters, addressed to "Dear Colleague," were signed by the "Coalition in Support of Breast Cancer Research." An investigation by **The Cancer Letter** determined that the group's address was misleading and its telephone number unlisted.

A telephone survey by **The Cancer Letter** determined that the coalition would have spent at least $4,500 to send its letters by overnight mail. Using the NSABP's volume discount rates would have reduced this expense by as much as half (**The Cancer Letter**, April 22 & April 29).

Other Investigations

Though the university has concluded its investigation, NIH has initiated another investigation of possible misuse of funds associated with the coalition's activities, sources said.

Pennsylvania law enforcement officials said to **The Cancer Letter** that they are investigating the allegation that the coalition has used a misleading address.

Though the coalition's correspondence was being delivered to a box at Mail Boxes Etc., located near the NSABP headquarters, the coalition's stationery represented its address as a "suite."

Last month, an anonymous caller claiming to speak for the coalition acknowledged to **The Cancer Letter** that the coalition's mailing address was, in fact, a mail box rather than a suite.

Since the word "suite" connotes offices as opposed to a mail box, Pennsylvania consumer protection law prohibits such representations and provides for penalties of up to $1,000 for every letter sent.

R. Lee Clark, M.D. Anderson Mastermind, Visionary Dies

R. Lee Clark, a masterful lobbyist and a surgeon who ran the Univ. of Texas M.D. Anderson Cancer Center for 32 years and oversaw the implementation of the National Cancer Act as a member of the President's Cancer Panel , died last week.

Clark, 87, who had colon cancer, died in the cancer center he had built.

In 1946, when Clark became its first full time director and surgeon-in-chief, M.D. Anderson was housed in a converted home on an estate south of downtown Houston. Several surplus barracks were trucked in and converted into inpatient and outpatient clinics, a research laboratory, and an air-conditioned operating room.

Until his retirement in 1978, Clark's firm hand was evident in all aspects of operation of M.D. Anderson: from plotting the future of the comprehensive cancer center, to making recruitment decisions, to helping his staff handle personal and professional problems.

"Dr. Clark lived for two things: one, curing cancer and, two, M.D. Anderson," Emil J Freireich, professor of hematology and oncology at M.D. Anderson, said to **The Cancer Letter**.

"There was no bureaucracy at M.D. Anderson," Freireich said. "There was no delay. He did not refer anything to committees. He could make a decision that you would hate, but he would make a decision."

Clark was a member of the President's Commission on Heart Disease, Cancer and Stroke that, in 1965, called for a campaign to combat these causes of death.

In 1970, Clark convinced Sen. Ralph Yarborough (D-TX), then chairman of the Health Subcommittee of the Senate Labor and Human Resources Committee, to establish a National Panel of Consultants to develop recommendations for expansion of federal support of cancer research.

As co-chairman of that panel, Clark influenced the drafting of the National Cancer Act. In 1972, after that legislation was enacted, Clark was appointed to the first President's Cancer Panel.

Clark was also the former national president of the American Cancer Society and former chairman of the Committee on International Collaborative Activities of the International Union Against Cancer.

A Texas native, Clark received a degree in chemical engineering from the Univ. of South Carolina and an MD from the Medical College of Virginia. He came to M.D. Anderson after spending four years in the Air Force as director of surgical research.

"Dr. Clark provided the inspiration and leadership that helped M.D. Anderson become one of the world's outstanding institutions devoted to cancer patient care, research, education and prevention," said Charles LeMaistre, who succeeded Clark as M.D. Anderson president.

Clark is survived by his daughter, Rabia Lynn Clark of Austin, TX; son, Randolph Lee Clark II of Bizbee, AZ; sister, Ilene Stiles of Victoria; and three grandchildren.

Women Surgeons: Resume The Prevention Trial Now

The National Surgical Adjuvant Breast & Bowel Project has been "intellectually honest" about side effects of the drug tamoxifen, six women surgeons wrote in a letter to House and Senate members.

The letter, dated April 19, was signed by Janet Osuch of Michigan State Univ., Susan Love of the Univ. of California at Los Angeles, Margaret Dunn of Wright State Univ., Jeanne Petrek of Memorial Sloan-Kettering Cancer Center, Laura Esserman of the Univ. of California at San Francisco, and Carol Slomski of Michigan State Univ.

Excerpts from the letter follow:

"The tamoxifen trial has had political enemies from its inception. There is nothing wrong with this. What the opponents do not do, however, is speak for all women everywhere. The average women in our practices are not paid lobbyists on the Hill, nor are they in any position to argue with the tamoxifen trial opponents, They are, however, concerned about the risks of their daughters, and willing to help advance knowledge about it.

"Our job right now is to speak to these women, and to speak for them as well. Tamoxifen is not a panacea by any means. Everyone, and especially all of the women participating in the trial are well aware of the risks of the drug.

"There is no question in our minds, at all, that the NSABP has been intellectually honest about the side effects of tamoxifen, and that the members and their patients have been informed in an orderly and appropriate way as knowledge of them has evolved.

"Of the women who consent to be participants, all of them sign a consent that they are willing to take the potential risks associated with tamoxifen in exchange for the benefit of advancing knowledge. It is not up to us to tell a woman that she should or should not take the potential risk to achieve the desired end. It is her choice. We feel very strongly about this.

"Our job is to give a true informed consent. We will be unable to do this if the opponents of the prevention trial prevail and the trial is discontinued.

"In fact, what is likely to happen if the trial is discontinued is that because many physicians think that there is enough evidence to suggest that tamoxifen can reduce breast cancer recurrence in women with the disease, tamoxifen will be prescribed to healthy women anyway.

"This will be done without knowing (1) whether it actually does work in healthy women to prevent breast cancer, and (2) without knowing the benefit-risk ratio. This would be a tragedy.

"What we find so hard to understand is why the opponents of the trial think that they know what is best for women. Do they agree that women should be truly informed, and that we should have data to back up that informed consent process? Do they really want us to continue in the paternalistic treatment of women that has been so pervasive in the past?

"We firmly believe that scientific knowledge must advance for women to have any choices at all.

"In a few short years, testing for the BRCA-1 gene will be available. What are we to say to women who test positively for the gene? It is a nightmare for us to think that all we will be able to offer our patients is close monitoring or bilateral prophylactic mastectomies. Right now, this is the cruel reality.

"Will we be forced to continue in this archaic mode? Do the opponents of the tamoxifen prevention trial want us to have to continue to communicate that no other choices exist?

"If tamoxifen is shown to reduce breast cancer risk, and the benefits outweigh the risks, wouldn't it be better to be able to inform women that they have choices other than follow-up or mastectomy?"

RFAs Available

RFA HL-94-014
Title: **Angiogenesis In Breast Cancer**
Letter of Intent Receipt Date: Aug. 1
Application Receipt Date: Sept. 13

The National Heart, Lung & Blood Institute's Div. of Heart and Vascular Diseases invites research grant applications for up to four years of support for research into breast cancer angiogenesis. The objective of this RFA is to encourage vascular biologists to apply their knowledge and skills to elucidate the mechanisms whereby breast tumor cells stimulate angiogenesis and control the structure and function of the tumor blood vessels. The ultimate goal is to identify strategies that offer possibilities for treating breast cancer by inhibiting the vascularization of tumors.

Trans-NIH Breast Cancer Collaborative Effort: This RFA is part of the activities to be initiated by NIH to advance knowledge regarding the etiology, treatment, and prevention of breast cancer.

Applications may be submitted by domestic and foreign for-profit and non-profit organizations. The R01 grant will be used. Total project period may not exceed four years. Approximately $1.5 million in total costs will be provided for the first year of support for the entire program. No more than eight grants will be awarded under this program.

The letter of intent is to be sent to: Dr. C. James Scheirer, Div. of Extramural Affairs, NHLBI, Westwood Bldg, Rm 557, Bethesda, MD 20892, Tel: 301/594-7452, FAX: 301/402-1660.

Inquiries: Dr. Constance Weinstein, Div. of Heart and Vascular Diseases, NHLBI, Federal Bldg, Rm 3C06, Bethesda, MD 20892, Tel: 301/496-1081, FAX: 301/480-6282.

RFA CA-94-017
Title: **Translational Investigator Grants For Cancer Prevention And Control**
Letter of Intent Receipt Date: June 15
Application Receipt Date: Sept. 23

NCI's Div. of Cancer Prevention and Control invites research grant applications from investigators new to this area of research, who are in the early stages of their career, to conduct studies translating phase I (hypothesis development) and II (methods development) basic, epidemiological, and clinical research into new approaches for the prevention and control of cancer. Applications may be submitted by domestic, non-profit and for-profit organizations. The Principal Investigator must have a doctoral degree and be working independently, but at the beginning stages of his or her research career in translational prevention and control research.

The NIH R01 grant will be used. Total project period may not exceed four years. Total direct cost may not exceed $500,000. The direct cost in any budget period may not exceed $150,000. Award date is July 1, 1995. Approximately $1.5 million, per year, in total costs for four years will be committed to fund eight awards.

Inquiries: Helen Meissner, Div. of Cancer Prevention and Control, NCI, Executive Plaza North Rm 330, Bethesda, MD 20892, Tel: 301/496-8520.