THE CANCER LETTER

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SWOG FIVE DRUG ADJUVANT BREAST STUDY SHOWS REMARKABLE SURVIVAL FOR OLDER, YOUNGER WOMEN

Southwest Oncology Group Chairman Barth Hoogstraten reported results this week of SWOG's adjuvant breast cancer study in which a combination of five drugs has produced two to four year disease free survival of 80-90%—even more remarkable, the rates are equally good for pre- and postmenopausal patients. (Continued to page 2)

In Brief

UPTON NOT PLANNING TO LEAVE NCI, AS HINTED BY CALIFANO, OVER NEW ETHICS REGULATIONS

NCI STAFF members are concerned about the impending regulation which would prevent most of them from accepting jobs with universities, medical schools or other research institutions which have NCI contracts or grants. They are not, however, being panicked into leaving before the regulation takes effect June 30, as HEW Secretary Joe Califano has indicated they might. The Ethics in Government Act goes into effect on that date; it would prevent a government employee from going to work within two years after leaving government for any organization with which his agency was dealing. That would have prevented former NCI executives such as Gordon Zubrod, Nathaniel Berlin, Palmer Saunders, John Yarbro, Paul Carbone and Steve Carter from accepting the positions they now hold with universities and cancer centers. Most NCI and NIH executives and scientists plan to eventually move into the academic world when they retire; Califano said they might leave immediately if that prospect is denied them. He also named NCI Director Arthur Upton and NIH Director Donald Fredrickson as among those who might go before June 30. ***The Cancer Letter*** learned, however, that Upton and other NCI staff members are not getting ready to bail out. They are counting on Congress to soften the act's impact, either with new legislation or a statement clarifying congressional intent . . . . **NURSES WORKING** in cancer research are exploring the prospect of starting a new association for their field. Rosemary Mackey, chemotherapy research coordinator at Memorial Sloan Kettering, and Susan Hubbard, with NCI's Medicine Branch, have organized a luncheon for May 15 at the New Orleans Hilton to go into the question. "We support the development of the Oncology Nursing Society as a group whose aims are to explore and improve nursing practices in cancer," Mackey said. "However, we feel there may also be room for an association of nurses involved in biomedical research." Renilda Hilkemeyer, M.D. Anderson, will speak at the luncheon on the role of the research nurse in clinical investigation. Div. of Cancer Treatment Director Vincent DeVita will moderate a panel discussion by Joseph Bertino, Emil Frei, Emil Freireich, and Irwin Krakoff. The date is the last day of the ASCO annual meeting and just prior to the AACR and Oncology Nursing Society annual meetings, all in New Orleans.

CMFVP GETS 80-90% SURVIVAL FOR BOTH YOUNGER, OLDER WOMEN IN SWOG STUDY

(Continued from page 1)

Those percentages are better than those of the Bonadonna CMF study at a comparable time. The Bonadonna results were good enough to lead to widespread use of CMF in clinical practice, at least for women under age 50.

Neither the Bonadonna study nor the L-PAM study by Bernard Fisher's National Surgical Adjuvant Breast Project showed any substantial improvement for postmenopausal women, although like CMF, L-PAM did gain startling improvement for certain groups of younger women.

SWOG's study compared melphalan (L-PAM) as a single agent with a five drug combination of cyclophosphamide, methotrexate, 5-FU, vincristine and prednisone (CMFVP). Hoogstraten reported these results this week at the opening session of the NCI Div. of Cancer Treatment Board of Scientific Counselors' long awaited clinical trials review:

More than 500 patients have been entered in the two arms, with up to four years time on study and two years median.

Melphalan—Patients with one to three positive lymph nodes, 80% disease free survival, both pre- and postmenopausal; patients with four or more positive nodes, premenopausal, 50% disease free survival, postmenopausal, 65%.

CMFVP—Patients with one to three positive nodes, 90% disease free survival; patients with four or more positive nodes, 80%, both pre- and postmenopausal.

Historically at four years following mastectomy, untreated patients with positive nodes have a 50-60% disease free survival rate.

In the SWOG study, CMFVP was administered on a weekly schedule. Bonadonna used an intermittent schedule, every three or four weeks depending on toxicity.

CMFVP is not a new combination; the same drugs made up the now famous Cooper regimen, which achieved 90% response in an advanced breast cancer study in the 1960s.

Another cooperative group, Cancer & Leukemia Group B, has been using CMFVP in an adjuvant breast study. Although CALGB has not put its data together yet, Hoogstraten said it is getting results similar to SWOG's.

James Holland, CALGB chairman, confirmed to ***The Cancer Letter*** that his group's study with CMFVP has found it equally effective for postmenopausal patients. He said the code has not yet been broken, so no figures are available.

"Although I have long held back the report, I still wonder whether it is too early to present it," Hoogstraten said. "Just how early or how late should results be reported in order to avoid undesirable bandwagon effects?

"It is important to realize that these results in no way at all decrease the value of the Fisher and Bonadonna studies. It is merely an evolution in clinical investigation giving rise to more questions which will need answers."

DCT Director Vincent DeVita, in remarks opening the two-day review of cooperative group and other clinical trials activities, called attention to a significant decrease in breast cancer mortality among white females under age 50 in the U.S. "I think we can attribute this to the widespread adjuvant trials," he said.

If the SWOG results hold up, there should be a further drop in the rate for younger women, and for the first time, a breast cancer mortality trend downward for women over age 50.

Presentations made at the review this week on trials in pediatric malignancies, lymphomas, sarcoma, special resource needs, funding and review mechanisms will appear in future issues of ***The Cancer Letter.***

TREATMENT PROGRESS REPORT TO KENNEDY INCLUDES NEW DRUGS, OTHER MODALITIES

Major new drugs developed or entered into clinical use during the 1970s were included in the report on progress in treatment of cancer NCI presented to Sen. Edward Kennedy's Health Subcommittee at its oversight hearings on the National Cancer Program (***The Cancer Letter***, March 23).

Adriamycin

This drug was discovered in Italy. NCI confirmed and extended preclinical studies in the early 1970s and sponsored clinical testing in the U.S. and elsewhere, which led to filing of a new drug application. The drug became commercially available in the U.S. in 1974 for treatment of breast cancer, leukemias, lymphomas, pediatric solid tumors, lung cancer, bladder cancer and sarcomas. All major clinical studies in these and other tumors were totally supported by NCI, at an estimated cost of $3 million. In addition, purchase of the drug for these studies has cost a total of $10.2 million since 1971.

Nitrosoureas (BCNU, CCNU, Methyl CCNU, Streptozotocin, chlorozotocin)

The synthetic nitrosoureas were developed entirely under NCI auspices. Two of these (CCNU and BCNU) became commercially available in 1976 and 1977 for treatment of brain tumors and Hodgkin's disease.

Streptozotocin remains investigational because its efficacy has been primarily confined to a very rare malignancy—islet cell tumors of the pancreas. The drug does induce striking remissions in patients with that tumor. Although the original discovery of streptozotocin was made by a pharmaceutical company, the discovery of biological activity and all further development was carried out under NCI auspices.

Chlorozotocin, a new analog not toxic to bone marrow, has recently been developed in an effort to reduce the toxicity of these drugs while preserving antitumor activity. Preliminary results confirm this

improved therapeutic ratio.

Clinical studies in the U.S. with these agents have been performed entirely with NCI support, costing approximately $3 million. In addition, one study from South Africa made use of drugs supplied by NCI and was supported in part by a grant in related areas. Development, production and other costs excluding clinical trials for all the nitrosoureas have amounted to approximately $7.5 million.

DTIC

This drug was developed totally by NCI. Most of the clinical trials that led to commercial marketing of DTIC in 1975 for the treatment of patients with advanced melanoma were conducted subsequent to 1971. The cost of preclinical development of the drug, including preparation and production of a formulated product for clinical trials, has totaled $2.6 million. Clinical trials over the years since 1972 are estimated to have cost $2 million.

L-asparaginase

The biological activity of guinea pig serum was discovered by Kidd in the 1950s and identified as due to the enzyme asparaginase by Broome in the 1960s. These early studies were partially supported by NCI. Most subsequent preclinical and all clinical studies were supported by NCI until the drug became commercially available for the treatment of acute lymphocytic leukemia in 1978. NCI purchases of this drug have totaled $1.8 million. Clinical trial costs are estimated to be $500,000.

Hexamethylmelamine

This drug was introduced into clinical trials by NCI in the early 1960s. Further development was not pursued because of apparent lack of good effects. Recent clinical studies, however, have shown hexamethylmelamine to be the most active drug in use for ovarian cancer. Its utility has also been more fully appreciated, as a result of studies on human tumors growing in immunodeficient mice, performed under NCI support which showed the rather startling activity of this drug in destroying these tumors. Poor absorption when the drug is taken by mouth and poor tolerance by patients because of nausea and vomiting has prompted development of a new soluble form which has just reached clinical trial.

Cis-platinum

The biological activity of cis-platinum was first observed by Rosenberg in the mid-1960s. Further development and production efforts were toally supported by NCI. Clinical studies began just after the passage of the National Cancer Act. In December 1978, this drug was approved for marketing for use in testicular and ovarian cancers where its efficacy has been impressive. These studies, as well as those in other diseases such as bladder cancer, carcinoma of the cervix and head and neck cancer were all carried out with drug produced by NCI. With two exceptions, all clinical studies with cis-platinum have also been carried out entirely with NCI support. Cost of production and formulation of this new agent by NCI has totaled $1.5 million and clinical trial costs are in the range of $1 million.

Daunorubicin

This antitumor antibiotic is related to adriamycin. Although the drug and early clinical studies originated in France and Italy, most current treatment schemes were developed in the U.S. and were totally supported by NCI. Studies supported by NCI clinical trials program since 1971 have confirmed its marked effectiveness against acute leukemia in adults, and it will soon be marketed for this purpose. Drug costs have been $1.5 million and clinical trials costs are in the range of $1 million.

5-Azacytidine

This drug was discovered simultaneously in Czechoslovakia and in the U.S. in 1967. The latter work was supported under NCI contract. Since 1971, this drug has had extensive clinical trials in the U.S. under NCI support, and its antileukemic activity as well as its optimal method of administration to circumvent nausea and vomiting were established in these trials. NCI purchases of this drug have totaled $530,000. Clinical trials costs are estimated at $500,000.

Bleomycin

The discovery and initial clinical studies with this drug took place in Japan in the 1960s. The drug became commercially available in the U.S. in 1974. Its marketing in the U.S. was based on clinical studies performed under NCI support during the early 1970s. Drug purchased by NCI for clinical studies totaled approximately $2.0 million. Clinical trials costs were approximately $2.0 million.

VP-16

This has been effective in the treatment of lymphoma, leukemia and small cell carcinoma in the lung. Sandoz Laboratories developed this drug in Switzerland as a derivative of drugs studied by NCI in the late 1940s and early 1950s. The clinical development of the drug has been supported entirely by NCI in the U.S. and partially in Europe through work done by EORTC and the Swiss Cancer Study Group. The drug has been supplied free to NCI, but clinical trial costs thus far are in the range of $250,000.

Tamoxifen

This is an antiestrogen drug which produces useful antitumor responses in patients with breast cancer without the usual side effects of hormones. It has recently been marketed in the U.S. Most of its development was by private industry; however, clinical trials using tamoxifen and a related antiestrogen were in part supported by NCI to the extent of about $200,000.

Aminoglutethimide

This compound which can completely suppress production of hormones by the adrenal gland appears to be able to replace surgery in advanced breast cancer where palliation with adrenalectomy is appro-

priate. This drug was initially developed by industry as an anticonvulsant. The drug's mechanism of action as an effective agent was elucidated totally through support from NCI's Breast Cancer Task Force. Its clinical usefulness was demonstrated in NCI-supported studies, which have cost approximately $500,000.

M-AMSA

This is the newest drug introduced by the Div. of Cancer Treatment's drug development program. Originally synthesized by Cain in New Zealand, all subsequent developmental work has been under NCI auspices. Even in its early stages of development, it has shown extraordinary promise as an antileukemic drug. Adult patients with acute leukemia treated with m-AMSA have attained complete remission after having previously failed all other drugs. Other antitumor effects have been noted and studies are in progress to determine m-AMSA's range of effectiveness. M-AMSA is almost devoid of the troublesome side effects of nausea and vomiting. Drug development and clinical trials have thus far cost approximately $1.5 million.

High-dose Methotrexate

The effectiveness of methotrexate was initially discovered by Sidney Farber in 1948. Its side effects on bone marrow can be reversed by "rescue" with the co-factor of the vitamin folic acid called citrovorum factor. Used in high, ordinarily lethal, doses, with rescue, its antitumor effect is magnified and its spectrum of activity different. These manipulations have been studied extensively in this decade following the initial clinical use of these "rescue" regimens by Djerassi. High dose methotrexate appears useful in the treatment of acute leukemia, lymphomas and osteosarcoma. Its usefulness in other diseases in a variety of schedules is currently under study. Very recently the nausea and vomiting associated with the use of high dose methotrexate has been shown to be preventable using tetrahydrocannabinol. Drug costs alone amount to $1.5 million annually for the past four years, with the cost of clinical studies thus far in the range of $500,000.

Delta-9-tetrahydrocannabinol

Anecdotal accounts from patients have suggested that smoking marijuana prior to receiving intravenous antitumor drugs resulted in a decreased incidence of nausea and vomiting induced by the antitumor agents. Using tetrahydrocannabinol supplied by the National Institute of Drug Abuse, investigators initiated clinical trials in 1975. The results of these preliminary studies are positive. To make this drug more widely available for clinical trials, NCI cross-filed NIDA's investigational new drug application in 1978 and has assumed the supply and distribution of drug to all trials previously supplied by NIDA. Total cost of these trials to the NCI to date has been $100,000.

Other new anticancer drugs with promise

Revision of NCI's drug development program in 1975 has resulted in the development of several new types of antitumor agents aimed at affecting slower growing more common human tumors. A major effort has also been aimed at developing new agents, or analogs of older agents, devoid of toxicity. While many of these drugs are just reaching the clinics, it is reasonable to assume they will replace their more toxic parent compounds since they are at least as effective as the parent compounds in rodent tumors. If so, they will represent significant clinical advances in cancer chemotherapy.

Some examples are: (1) PALA, a unique antimetabolite which has completed phase I testing in man; (2) 2'-deoxycoformycin, a specific inhibitor of enzymes on the surface of lymphocytes which may be useful in acute leukemia without suppressing normal marrow; (3) an aziridinylquinone derivative, a new drug with unusual brain penetration and extraordinary activity against intracranial tumors in mice; (4) thymidine, a pyrimidine base (a normal body constituent) capable of inhibiting the growth of human tumors in mice without the usual side effects of other antitumor drugs, which is in early trials; and (5) interferon, an antiviral compound which is a natural body constituent, as well as poly I-C-polylysine, a synthetic inducer of interferon, both of which are under study.

Second-generation less toxic compounds include AD-32, developed at the Sidney Farber Cancer Center, and aclacinomycin, developed in Japan. Both are related to adriamycin. Neither of these drugs appears to have cardiotoxic effects, and in addition aclacinymycin does not cause hair loss. A new malonate derivative of the recently marketed platinum compound, which is devoid of the severe emetic effects of the parent compound, has recently been developed. Pentamethylmelamine, a soluble derivative of hexamethylmelamine, should obviate the gastrointestinal toxicity of hexamethylmelamine.

The NCI report described developments in other treatment modalities:

Radiotherapy

1. High linear energy transfer (LET) program

A. Neutrons: This year NCI will establish three medically dedicated neutron generators in cancer centers to overcome technical limitations of the use of older physics machines. Neutron radiation for therapy was originally introduced to treat cancer by Robert Stone, John Lawrence and Paul Aebersold (Univ. of California, 1940). This form of radiation may have considerable biological advanta ge over conventional radiotherapy because of lesser reliance on the proper exygenation of malignant cells. Progress was delayed by unexpected toxicities and technical difficulties. Catterall in England, using primitive equipment, rediscovered the therapeutic potential of neutrons in the 1970s. Current development of neutron generators practical for cancer treatment

began totally under NCI support and now extends to five institutions. Preliminary results indicate this form of therapy may achieve a higher percentage of total eradication of localized tumors with the greatest success reported in the treatment of salivary gland tumors and other tumors of the head and neck region.

The U.S. through NCI support has assumed the leadership in the development of neutron generators for medicine. An increase of $9 million is projected for expansion of this project in 1979 to include two new generators to expand clinical trials using this equipment.

B. Other particles: Other forms of high LET radiation are under investigation. Favorable clinical results have been reported with the use of protons in tumors of the eye treated at the Massachusetts General Hospital. Extent of NCI funding for research cited: $13,735,000, 1972-1978.

2. Radiosensitizer/radioprotector program

A program was instituted in 1977 for development and clinical testing of radiosensitizer drugs. One compound reached the clinics in late 1977. Clinical trials are being conducted in the treatment of brain tumors, head and neck cancer, esophageal cancer, bladder cancer, and pancreatic cancer which currently rank among those tumors least amenable to surgery or conventional radiation. Preliminary clinical experience with this compound together with radiation is favorable. The radiosensitizers were initially developed by Roche Laboratories in England, and the early research work in clinical trials was also done in England, with some NCI grant support.

NCI is currently providing $1.5 million annually for development of radiosensitizers/radioprotectors. The testing of these compounds in comparative trials against conventional treatments amounted to $500,000 in 1978, and with increasing applications will require $2 million in 1979. All stages subsequent to the initial idea have been 100% supported by NCI. Extent of NCI funding for research cited: $395,000, 1977-1978.

3. Computerized tomography and treatment planning

Computerized tomography, introduced by a British corporation, is the latest innovation in radiotherapy planning permitting safe delivery of increased dosages to tumors to increase curability while minimizing damage to normal structures. Developmental efforts did not receive NCI funds. Implementation and refinement of this use of scanning were supported in part by NCI.

HLA typing and transfusions

Patients with leukemia and aplastic anemia receiving multiple transfusions become immunized and refractory to platelet and granulocytic transfusion from random, non-matched donors. The routine use of platelet typing has been a significant advance in supportive care since 1971. Large computerized files of specifically types (HLA types) platelet donors are now available in many centers, and an active exchange of HLA-typed platelets takes place among hospitals throughout the country in a program initiated and coordinated by NCI. The increased availability of HLA-typed platelets has markedly decreased the incidence of fatal hemorrhage in leukemia and aplastic anemia and studies are in progress to determine if initial transfusions of specifically HLA-matched platelet preparations can totally prevent the development of immunization.

Improved techniques of cryopreservation of platelets has allowed the creation of banks of frozen HLA-typed platelets, thereby decreasing the burden of the donors and maintaining a supply for emergency use. The initial development of HLA typing of platelets came out of intramural NCI programs supported by additional contract facilities ($450,000 annually since 1971).

The use of white blood cell (granulocyte) transfusions to treat infections

White blood cells are difficult to separate efficiently from whole blood. The clinical application of granulocyte transfusions depended on the development of a variety of mechanical devices which can safely process large volumes of blood from normal donors. A number of such techniques have become commercially available before and since 1971 and have facilitated the definition of clinical trials testing the efficacy of white blood cell transfusion.

Granulocyte transfusions have now been shown to treat successfully bacterial infections otherwise resistant to antibiotic therapy alone. Granulocyte transfusions have become an important part of the management of patients with leukemia and are now available throughout the country supplied by regional blood centers. In addition to the treatment of established infections, preliminary results of a recent study suggest that granulocytes administered prophylactically can prevent the development of serious, often fatal infections in patients receiving intensive chemotherapy. If confirmed this observation could appreciably reduce the morbidity associated with leukemia treatment. Extent of NCI funding for research cited: $3,349,000, 1972-1978.

Bone marrow transplantation for acute leukemia

Bone marrow transplantation has now been shown to produce long term disease free survival in a small fraction of patients with drug resistant acute leukemia who have siblings with similar tissue typing characteristics. In this population, improvements in pretransplant histocompatibility testing have markedly reduced early marrow rejection, while advances in supportive care have decreased the frequency of early hemorragic or infectious deaths.

Many institutions are now studying the role of transplantation during remission of the leukemia in patients with suitable donors. In addition it has been demonstrated that autologous bone marrow, taken

during remission and frozen, can accelerate recovery of the patient's bone marrow after thawing and transfusion, and can allow the delivery of more intensive drug therapy. This technique of marrow cryopreservation of autologous marrow is now fairly simple and eliminates the problem of graft reactions. It is presently being studied in patients with leukemia, other hematologic malignancies and certain types of lung cancer.

NCI has supported all the work in bone marrow transplantation in the U.S. The seminal contributions were made at the Univ. of Washington by E. Donnel Thomas and his group. Extent of NCI funding for research cited: $11,895,000, 1972-1978.

Limb salvage surgery

Application of systemic treatment has made an impact on the need for radical limb surgery. En bloc resection of bones affected with malignancies instead of amputation has also been rendered possible by surgical innovations and the availability of prostheses. The use of chemotherapy in osteosarcoma and radiotherapy and chemotherapy in soft tissue sarcoma of the extremities is increasingly reducing the need for amputations, while still achieving cures.

Development of these surgical techniques took place in cancer centers such as Memorial, Mayo, Sidney Farber, and UCLA under NCI support. The intramural NCI program pioneered the work on soft tissue sarcoma. Extent of NCI funding: $5,005,000, 1972-1978.

Surgical staging (laparotomy and laparoscopy) and other staging techniques

Techniques have been perfected in determining the extent of malignant disease in the abdomen through surgical staging and second look procedures that have improved other approaches to treatment. For example, in the lymphomas, patients undergoing these surgical procedures can be spared unnecessary radiotherapy. Surgical and radiologic staging studies and second staging operations in testicular cancer, melanoma, ovarian cancer, and small cell lung cancer are proving important in treatment planning.

The pioneer work in staging of lymphomas took place at Stanford Univ. and in the intramural NCI program in the late 1960s and early 1970s. They are now widely applied in clinical trials. Extent of NCI funding: $1,399,000, 1972-1978.

Surgical treatment of metastatic disease

Surgical resection of metastases was once considered fruitless and radical. Surgical oncologists have now documented improvement in survival in appropriately selected patients. In high risk groups, such as patients with osteosarcoma, early detection of metastases followed by removal of many lesions with staged sequential resections now indicates that cures are possible even in patients previously considered hopeless. Chemotherapy may also play a role in rendering these lesions amenable to surgical resection. In testicular cancer chemotherapy has been reported to convert some malignant tumors to a more benign teratomatous tumor which can subsequently be resected.

Pioneer work was done in the NCI intramural surgical program. Support of similar surgical oncology projects has been totally supported by NCI at cancer centers. Extent of NCI funding: $3,655,000, 1972-1978.

Total parenteral nutrition

Mortality in cancer operations has been reduced by improving the nutritional support of the cancer patients. These innovations were introduced by surgeons with a strong interest in cancer treament; this type of support has subsequently become widely applied. More recently, interest has been stimulated to evaluate total parenteral nutrition's usefulness in modifying toxicity during intensive chemotherapy.

NCI has provided support for total parenteral nutrition research in its intramural programs. In addition, $1.4 million annually is devoted to evaluating the usefulness of total parenteral nutrition in treatment in the extramural program.

Immunotherapy

Since 1972, a sizable effort has been devoted to testing the effect of boosting immune defenses against tumors. While in general results with nonspecific immunotherapy, such as BCG, have been disappointing, there are exceptions when BCG has been combined with other treatment modalities, usually chemotherapy. Encouraging results have been reported with acute leukemia, melanoma, and lung cancer with use of BCG. Other immunostimulants such as levamisole and thymosin have recently been reported to improve survival of treated patients. These pilot studies require confirmation, and such trials are in progress. If positive, they will represent a significant advance in cancer treatment. Extent of NCI funding: $725,000, 1974-1978.

ADVISORY GROUP, OTHER CANCER MEETINGS FOR APRIL, MAY

National Conference on Urologic Cancer–1979–April 4-6, Los Angeles Hilton, sponsored by American Cancer Society.

Clinical Cancer Program Project Review Committee– April 9-11, NIH Bldg 31 Rm 6, open April 9, 8:30-10:30 a.m.

Pancreatic Cancer Project Review Subcommittee– April 11, Dallas Hyatt Regency, open 8:30–10 a.m.

The Physician and Oral Cancer– April 12, Roswell Park continuing education in oncology.

Advances in Hematology & Oncology– April 23-26, New York Hospital-Cornell Medical Center.

Biometry & Epidemiology Contract Review Committee–April 25, Landow Rm A open 8:30–9 a.m.

Div. of Cancer Biology & Diagnosis Board of Scientific Counselors– April 27-28, NIH Bldg 31 Rm 7, open April 27, 9 a.m.–5 p.m.

International Society of Clinical Biostatisticians– May 2-3, Institut Jules Bordet, Brussels.

EORTC Symposium on Progress & Perspectives in Lung Cancer Treatment– May 3-5, Brussels.

Breast Cancer Task Force– May 3-4, NIH Bldg 31 Rm 10, 1-5 p.m. May 3, 8:45 a.m.–adjournment May 4, all open.

Tumor Immunology Committee– May 7-8, NIH Bldg 31 Rm 9, open May 7, 9–9:30 a.m.
The Changing Scene of Childhood Cancer–May 9, Hartford, Conn., sponsored by American Cancer Society Connecticut Div. and Yale Comprehensive Cancer Center.
Immunotherapy of Cancer: Success or Failure?– May 10, Roswell Park continuing education in cancer.
Cancer Research Manpower Review Committee–May 13, New Orleans Hilton, open 9–9:30 a.m.
15th Annual Meeting of the American Society of Clinical Oncology– May 14-15, New Orleans.
Role of the Research Nurse in Clinical Investigation– May 15, noon, New Orleans Hilton.
70th Annual Meeting of the American Assn. for Cancer Research– May 16-19, New Orleans.
Fourth Annual Congress of the Oncology Nursing Society– May 17-19, New Orleans.
National Cancer Advisory Board– May 24-25, NIH Bldg 31 Rm 6 (Schedule to be announced later).
NCAB Subcommittee on Centers–May 24, NIH Bldg 31 Rm 11A10, open 9–10 a.m.
NCAB Subcommittee on Planning & Budget–May 24, NIH Bldg 31 Rm 10, 7:30 p.m., open.
NCAB Subcommittee on Carcinogenesis– May 24, NIH Bldg 31 Rm 10A34, 10:30 a.m., open.
NCAB Subcommittees on Special Actions and on Construction– May 24; entire meetings for both will be closed.
Clearinghouse on Environmental Carcinogens Chemical Selection Subgroup–May 25, NIH Bldg 31 Rm 7, 9 a.m., open.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Address requests to the contract officer or specialist named, NCI Research Contracts Branch, the appropriate section, as follows:
Biology & Diagnosis Section and Viral Oncology & Field Studies Section–Landow Building, Bethesda, Md. 20014; Control & Rehabilitation Section, Carcinogenesis Section, Treatment Section, Office of the Director Section–Blair Building, Silver Spring, Md. 20910.
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CM-97252

Title: *Screening of compounds using human tumors in athymic mice*
Deadline: *Approximately May 11*

NCI is seeking organizations with the capabilities and facilities (1) for maintaining and operating a small colony of athymic mice; (2) producing animals to carry and maintain tumor lines for testing; (3) maintain a limited frozen tumor bank to provide backup for tumor lines; and (4) conduct the testing of compounds by means of a panel of in vivo transplantable tumor test systems.

To be considered for award, respondents must meet the following minimum qualifications:

(1) Experience in conducting in vivo screening programs; (2) understanding of the project's workscope; (3) previous experience and current ability to breed and house healthy athymic mice in sufficient quantities to carry out the project; and (4) facilities which include an existing barrier for housing animals.

This animal facility shall include, as a minimum, an absolute air filtration system, mechanical cage washing machines, auxilliary power sources, autoclaves (steam sterilizers) with sufficient capacity for handling large volumes of caging equipment and animal feed and bedding. Other facilities required are for (1) the conduct of studies of xenographs in athymic mice, (2) tumor transplantation, (3) drug preparation and administration, (4) conduct of biological characterization studies and (5) the operation of limited human tumor banks.

It is anticipated that one award will be made for a three year incrementally funded period.

Contracting Officer: Daniel Abbott
Cancer Treatment
301-427-8125

RFP NO1-CM-97249-14

Title: *Structure-activity studies among anticancer agents. Linear free energy relationships*
Deadline: *Approximately May 15*

The Laboratory of Medicinal Chemistry & Biology, Div. of Cancer Treatment, is seeking organizations not affiliated with chemical or pharmaceutical industries, having capabilities and facilities for the study of structure-antitumor activity relationships among members of various classes of antitumor agents. The approach to be applied in this project is the use of linear regression analysis to develop linear free energy relationships (LFER).

The objective of the project is the use of the correlations developed to suggest structural modifications which will maximize antitumor activity and/or minimize toxic side effects within a series of congeners. The contractor will be expected to apply LFER techniques which are suitable to NCI chemical and biological data. It also will be expected to apply the synthetic and analytical techniques necessary to measure any required chemical and physical parameters, e.g., partition coefficients, electronic and steric constants, where they are not already available in literature.

The contractor will be expected to develop correlations within drug classes selected by the project officer. Antitumor data may be furnished by the project officer or be available from another source. When correlations are developed, the contractor will be expected to provide suggestions with respect to possible drug modifications. The principal investigator must have extensive experience in LFER structure-activity correlations and substantial experience in the area of drug design together with evidence of the successful application of quantitative structure-activity techniques.

It is anticipated that the total project will require two technical man years of effort per year.

Contract Specialist: Susan Hoffman
Cancer Treatment
301-427-8125

RFP NCI-CM-97271

Title: *Studies concerning the role of hormone receptors in endometrial carcinoma*

Deadline: *May 11*

NCI requires an organization with a multidisciplinary team to conduct studies on patients with endometrial carcinoma.

The objectives of this three year study are: to determine the usefulness of steroid hormone receptors in predicting disease free interval, and survival of patients with adenocarcinoma of the endometrium; to determine the usefulness of estrogen and progesterone receptor concentrations in identifying patients with recurrent or advanced adenocarcinoma of the endometrium.

A standardized protocol will be developed by the successful contractors and the project officer. Single institutions must accrue 30 patients per year with primary untreated endometrial cancers and 10 patients per year with recurrent or advanced endometrial cancer. With regard to multi-institutional proposals, each institution must meet the minimum patient accruel figures.

Personnel proposed for this project must include a gynecologic oncologist and a senior level investigator familiar with steroid biochemistry and receptor methodology.

Contract Specialist: Charles Lerner
Cancer Treatment
301-427-8125

RFP NCI-CM-97260

Title: *Quick reaction synthetic chemistry work orders*

Deadline: *Approximately May 5*

The Drug Synthesis & Chemistry Branch, Div. of Cancer Treatment, wishes to establish quick reaction work order contracts with organizations having the capability to synthesize a variety of organic and inorganic compounds. Quick reaction contracts are master contracts competitively negotiated and awarded to more than one contractor. These contracts are designed to accomplish a specific task as rapidly as possible.

The objectives of the quick reaction contracts will be: 1) the resynthesis of known compounds of varying degrees of complexity, and 2) the synthesis of novel analogs of leads for structure-activity optimization studies. Compounds to be synthesized include nitrogen, oxygen and sulfur coordination fully characterized as to identity and must conform to the level of homogeneity and purity as required. In general, synthesis of 2-10 grams of each compound will be required.

To meet these needs, DCT is seeking organizations with the skill and facility to perform a variety of chemical reactions, and which can demonstrate innovativeness and proficiency in developing synthetic methods where existing methods are not practical.

Multiple contract awards are anticipated. Contracts will be awarded on a cost-reimbursement basis with individual work orders being awarded on completion or level of effort as determined by the contracting officer.

Contracting Officer: John Palmieri
Cancer Treatment
301-427-8125

RFP NO1-CO-95447

Title: *Cancer Communications Program support*

Deadline: *April 11*

The Office of Cancer Communication of NCI is soliciting proposals for a firm to provide communications services to support its effort to motivate the public to decrease risk of cancer and increase chances of recovery through the use of communications techniques. Program emphasis shall be through the use of "access" groups; that is, to reach large numbers of people through intermediary organizations. This is not a mass media program.

Offerors shall be limited to those firms having operating facilities within a 35 mile radius of Bethesda, Md.

Note: This notice is an amendment to an RFP announcement in the Feb. 23 issue of ***The Cancer Letter.*** This proposed procurement is a total set-aside for small business concerns.

Contract Specialist: Kris Boyer
Office of Director
301-427-7984

RFP 200-79-0921

Title: *Smoking and health education program for youth*

Deadline: *May 28*

Select, perfect, replicate, and evaluate five smoking and youth demonstration projects.

Contracting Officer, PGO
Center for Disease Control
255 E. Paces Ferry Rd. N.E.
Atlanta, Ga. 30305

The Cancer Letter _Editor Jerry D. Boyd

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