THE CANCER LETTER

Vol. 11 No. 29
July 19, 1985

Subscription $150 year North America
$175 year elsewhere

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CDC AWAITS RESULTS OF VIRAL CULTURES OF BAHAMA'S SERUM FOR AIDS CONTAMINATION BEFORE TAKING ACTION

The Centers for Disease Control plans no action on reports of HTLV-3-contaminated serum obtained from Laurence Burton's Immunology Researching Center in the Bahamas until the presence of HTLV-3 can be confirmed by viral cultures currently underway at the agency, a CDC

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"The President Has Cancer"

NCI SURGERY CHIEF BREAKS THE NEWS TO REAGANS AND THE WORLD AS CHIEF SPOKESMAN AFTER SURGERY

Until last weekend, Steven Rosenberg was only one of the better known surgical oncologists in the country, more recently for the fascinating research he has been doing in developing "adoptive immunotherapy" for the treatment of cancer. Thanks to the enthusiasm of Armand Hammer over the promising but very early clinical results of that research, Rosenberg came to the attention of the White House, but nothing like the scale that was generated last weekend. Now, Rosenberg probably is the most famous cancer surgeon in the universe.

Rosenberg was asked to join the team of surgeons who removed two feet of President Reagan's right colon July 13 because of his expertise in colon cancer (It had nothing to do with the possible use of adoptive immunotherapy in any future treatment program for the President). It quickly developed at the press conference following the surgery that Rosenberg was the member of the team at whom most of the reporters' questions were directed. The same pattern held at the press conference Monday when the fact that the tumor was malignant was made known.

The 44-year-old chief of the NCI Surgery Branch, in the Clinical Oncology Program of the Div. of Cancer Treatment, performed with cool, articulate detail the task of informing the world that for the first time in its history the sitting President of the United States had cancer (or at least the first time such was publicly known). A half hour earlier, Rosenberg had so informed Mrs. Reagan and then the President. Both took the news calmly and in good spirits, Rosenberg said.

Among the other information Rosenberg passed along in response to scores of questions from the press:

*He would not recommend any adjuvant therapy for the President because the surgery itself had a better than 50 per cent chance of being curative and because no regimen tested so far has proven effective in improving survival for colon cancer. However, he had discussed adjuvant therapy with NCI Director Vincent DeVita and would seek additional opinions on the possible use of chemotherapy.

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KATTERHAGEN SEEKING MORE SAMPLES FROM BAHAMAS TO TEST FOR HTLV-3

(Continued from page 1)

spokesman told **The Cancer Letter** July 16.

Results from the cultures are expected to be ready in several weeks, he said. According to CDC, confirmational testing of the samples by the Western Blot electrophoresis technique was "uninterpretable," so the agency decided to conduct additional tests of the sera.

Gale Katterhagen, director of oncology for Multicare Medical Center in Tacoma, submitted the samples to CDC for confirmational testing. Katterhagen and S.J. Insalaco, Pierce County Blood Bank director, tested the samples using a commercially available ELISA (enzyme-linked immunosorbent assay) test from Abbott Labs. They found eight of the 18 samples positive for HTLV-3, the virus associated with AIDS. All 18 samples were positive for hepatitis.

Gregory Curt, deputy director of NCI's Div. of Cancer Treatment, said, however, that "it's impossible to overlook even equivocable results." He said that the fact that the tests were equivocable "is very important" because both the ELISA and Western blot tests are designed to detect the presence of HTLV-3 antibodies in blood, not fractionated plasma protein products.

The samples were received from two patients who had visited Burton's Immunology Researching Center in Freeport. Blood from both patients tested positive for HTLV-3, Katterhagen reported (**The Cancer Letter** July 12).

Katterhagen is in the process of trying to obtain more samples of serum from patients who have been to the clinic in order to perform additional tests for HTLV-3 antibodies. He has also submitted a letter detailing his findings to the "Journal of the American Medical Assn." following the failure of the "New England Journal of Medicine" to publish reports of the tests as a letter to the editor.

Patients at the Bahamas clinic reportedly receive "immunoaugmentive therapy" consisting of injections of sera from multiple sources. Following the removal of blood from patients, serum is produced by fractionating plasma proteins by centrifugation and organic solvent extraction.

Curt said that Burton is known to have been treating AIDS patients since 1983.

To date, the Bahamas government has received no official report of HTLV-3 contamination of sera from the clinic and therefore, had no comment, an embassy spokesperson told **The Cancer Letter.**

Curt drafted a letter July 16 to Bahama Ministry of Health medical officer V.T. Allen informing her of the test results and recommending quality control measures for the clinic. A similar letter will be sent to Burton.

Curt would like to see diplomatic relations between the two countries used to obtain a list of patients who have visited the clinic in order to allow for followup in the U.S.

Although the Food & Drug Administration has no jurisdiction over the clinic's activities in the Bahamas, it has issued releases in the past advising the public of the risk of hepatitis reported at the clinic. Federal law prohibits bringing unapproved drugs such as the serum into the U.S., but government officials acknowledge the enforcement difficulties faced by customs inspectors.

Neither Burton nor any of the medical doctors associated with the clinic were available for comment. Speaking on behalf of the clinic, Betty Abernathy, who says she has been a patient at the facility for five years, said "the rumors are false" and that Burton had informed her that "no patient has ever come down with anything" from the sera.

ROSENBERG RECOMMENDS NO ADJUVANT THERAPY FOR PRESIDENT IS NEEDED

(Continued from page 1)

*Neither would he recommend therapy involving monoclonal antibodies at this time because that is "highly experimental" and also because "there is no role for it given the stage of the disease." Presumably, that also would apply to adoptive immunotherapy, although he was not asked about that procedure. Hammer had told White House Science Advisor George Keyworth about the promising results Rosenberg had observed in the first few patients who had received adoptive immunotherapy. Keyworth said if similar results could be obtained with 20 patients, he would ask the President for additional money to support large scale clinical trials. Apparently, the titillating prospect that the President himself might be the 20th such patient will not become a reality.

*He would not criticize the decisions made last year and last March, delaying colonoscopy or barium enema which might have turned up malignant tumor from four to 14 months earlier. He insisted it was "impossible" to say whether the tumor, classified as Dukes B, might have been Dukes A last year. He presented a clear, concise explanation of the differences between Dukes A, B and C.

*He defended the hemacult test as "one of the best and most practical tests for colon cancer" and although it has its problems, "is very useful."

*He said that since the President's diet during his 74 years "has served him well," he would recommend that he return to it. However, he would also recommend to anyone a reduction in fat and increase in fiber.

Rosenberg, responding to a question, insisted that "no one has told me I can't discuss any aspect of this case" with the press.

LaSalle Leffall, chairman of surgery at Howard Univ. Cancer Center, a member of the National Cancer Advisory Board and former president of the American Cancer Society, touched on what may be a significant aspect of the President's illness when he was interviewed on Cable News Network.

"Something good may come out of this," Leffall said. "It may start many of us to thinking about this disease, and go in for examinations. There is no question in can help make people aware of it throughout the world."

Examinations leading to diagnosis of colon cancer at Dukes A stage rather than Dukes B means five year survival of more than 90 per cent compared with more than 50 per cent.

More than a few oncologists have been shaking their heads this week, wondering what might have been in the President's case.

PRIVATE DEVELOPMENT OF FREE STANDING CANCER CENTERS CONTINUES MOMENTUM

The increasing private sector role in outpatient cancer care is evidenced by the growing number of for-profit freestanding cancer centers (FCCs) being established or under development throughout the country.

The New Jersey-based Comprehensive Cancer Care Corp., which claims to be the first publicly traded cancer care company, plans to open its second outpatient cancer clinic in West Orange, N.J. in September. The firm opened its first FCC in Lake Arrowhead, Calif., in March and expects to have between four and six centers operational by the end of the year. Virginia may be the site of a third center.

Known as the San Bernardino Mountain Cancer Medical Clinic, the Lake Arrowhead center was opened in association with Loma Linda Univ. School of Medicine oncologist Dennis Hilliard.

CCCC has no plans for formal affiliations with neighboring institutions, but will rely upon the hospital admitting privileges of physicians practicing at an individual center.

The firm's new West Orange facilitiy will include MDs with admitting privileges at neighboring St. Barnabus and Beth Israel Hospitals, Matthew Smith, CCCC vice president for marketing and operations told **The Cancer Letter.**

The company does not employ physicians directly, but provides management services to the physicians' professional corporation, including marketing, billing and reimbursement, personnel, accounting, equipment and pharmaceutical supplies. CCCC offers limited partnerships to MDs for the centers' buildings and radiation equipment.

Approximately 11 per cent of Comprehensive Cancer Care's stock is publicly held, with the remaining 89 per cent held by the firm's parent company, Continental Health Affiliates. CHA provides home health care services such as enteral and parenteral feeding, as well as outpatient hemodialysis.

The Los Angeles based Comprehensive Cancer Centers Inc., a wholly owned subsidiary of Salick Health Care, recently announced that it will take over operations of Cedars-Sinai Medical Center's radiation therapy department by Aug. 1. The company plans to open a 50,000 sq. ft. comprehensive cancer center at Cedars-Sinai by summer of 1986.

CCCI plans to establish a national network of cancer care networks, each consisting of a tertiary care center affiliated with a teaching hospital, "mini centers" for treatment in outlying community hospitals and satellite screening and detection facilities.

The company completed its first public stock offering in March, raising approximately $13.5 mil. through the sale of 1.07 mil. shares of common stock, Salick Health Care Chairman Bernard Salick told **The Cancer Letter.**

Salick announced an agreement in principle with American Medical International Inc. to jointly develop at least three cancer care networks at a cost of approximately $15 million each. AMI owns, operates and develops hospitals around the world and provides a variety of health care services to more than 500 communities.

The two companies plan to jointly finance the first network, with partial project financing through traditional private financing mechanisms, Salick said. The second and third centers will probably rely exclusively on straight project financing, he said.

Salick plans to establish as many as 20 such networks over the next two or three years, either independently or in cooperation with other firms. Each center will be linked by computer (**The Cancer Letter** Jan. 11).

CDP Associates, a La Jolla-based consulting firm that designs and constructs university-based cancer centers, community-based radiation centers and medical facilities management, is currently in the process of acquiring its former spinoff Health Corp., which already had five FCCs in operation by the beginning of the year, CDP's C.D. (Dunc) Pruitt said.

Renamed Intercommunity Cancer Centers of America, the firm now has seven FCCs in operation, and another three scheduled to open within the next six months. Pruitt expects to have an additional five centers open by the beginning of 1987, for a total of 20 centers within the next two years.

CDP itself has been involved in "at least" 26 FCCs to date, Pruitt said, adding that the firm will develop centers for parties interesting in operating the facilities themselves.

Not everyone is pleased with the development of private, for profit cancer treatment centers. Virgil Loeb, St. Louis medical oncologist and a member of the Board of Scientific Counselors of NCI's Div. of Cancer Prevention & Control, objected to what he thought was an endorsement of commercial free-standing cancer centers by NCI Director Vincent DeVita. DeVita had said they perhaps were the "missing ingredient in cancer treatment."

"Free standing cancer centers do not necessarily represent quality," Loeb said earlier this year at a DCPC Board meeting. "You can't franchise cancer care like hamburgers."

Charles Cobau, Toledo oncologist and also a DCPC Board member, had a different opinion. "It seems to me that the concept of freestanding cancer centers has already been established in a number of communities. My view of freestanding cancer centers is that they can make a major contribution in a positive way to cancer care. I support the idea that they be strongly encouraged to affiliate themselves with clinical research and work through NCI. During the next decade or two, freestanding cancer centers may end up caring for a majority of patients."

LITERATURE REVIEW SUPPORTS NEED FOR MORE CANCER CONTROL RESEARCH

A cancer control literature review conducted by Peter Greenwald, director of NCI's Div. of Cancer Prevention & Control, sifted through 4,700 literature citations and turned up 122 English language papers "from anywhere in the world identified as meeting our definition of cancer control," Greenwald told the DCPC Board of Scientific Counselors.

The largest group of intervention studies were educational. Nineteen of 31 described research on breast self examination. Twelve of the 20 screening papers also dealt with breast cancer, three with colorectal cancer, and the others were cervix, lung, stomach and skin cancer.

"The published human chemoprevention papers, while very preliminary, give hints of activity of chemopreventive agents in people," Greenwald said. Thus, taken together, they provide further reason to maintain our emphasis in this field. For example, Gouveia, et al, in France bronchoscoped and took 10 biopsies before and after treating heavy smokers with aromatic retinoid, etretinate. Ten of 11 volunteers who completed the protocol had a lower index of metaplasia at the end of the study.

"Stich, et al, studied betel nut/tobacco chewers from a mountain tribe in the Philippines. Four groups of study subjects were given vitamin A capsules (150,000 IU/week), betacarotene (180 mg/week), canthaxanthin ((180 mg/week) or placebo. Before and after nine weeks of treatment, the buccal mucosa was scraped with a tongue depressor and the micronucleus test performed. A reduction in the number of micronuclei was seen in 24 of 26 in vitamin A and 22 of 25 on betacarotene. No reduction was seen in the canthaxanthin or placebo groups.

"Shaw working with BSC member Jerome DeCosse and others treated patients having leukoplakia with throat lozenges containing 13-cisretinoic acid for a six month period. Decrease in size of leukoplakia or complete clinical disappearance was seen in nine of 11 who finished the protocol, although the leukoplakia tended to recur after the study was ended.

"Dion, et al, showed reduction in stool mutagenicity after ascorbic acid and alpha tocopherol, and mixed results were seen in early studies to prevent recurrence of bladder cancer. Several of these studies used tests which are yet to be validated as markers of decreased cancer incidence, and as mentioned, all of the reports thus far are very preliminary.

"Unfortunately, many of the 122 cancer control studies show major methodologic flaws, particularly the educational intervention studies. Only seven of the 31 of these controlled for confounding. My opinion is that in all, there were at most 15-20 studies that would be considered solid contributions to the cancer control literature. Much of the rest is not the type of work that we would like to support. This analysis is not quite complete, but I think we can conclude that there is an important need for continuing emphasis on developing cancer control as a research field and on continuing to build a critical mass of investigators in this field."

Greenwald said the literature review "should provide a baseline against which to judge our future progress in cancer prevention and control. The studies DCPC has supported in the last two-three years generally are not yet published."

AACR PROGRAM COMMITTEE LISTS 10 PAPERS FROM 76TH ANNUAL MEETING

The American Assn. for Cancer Research usually does not list what may be considered the "best" or "among the best" papers presented at its annual meetings, but at the 76th meeting in Houston, 10 papers were selected as "papers of interest recommended by the Program Committee." They were (as excerpted from the abstracts):

Unique Ha-ras alleles in tumor and leukocyte DNA of cancer patients. Theodore Krontiris, Nancy DiMartino, Mark Colb and David Parkinson, Tufts Cancer Research Center.

The highly polymorphic Ha-ras locus may be quite useful as a marker for inherited susceptibility to cancer. Twenty four allelic restriction fragments have thus far been detected by Southern blotting of white blood cell and tumor DNAs of unrelated Caucasians. Fifteen of the 24 alleles have only been detected in cancer patients ($p<0.001$). Family studies and analysis of matched tumor/WBC DNAs indicate that these rare alleles are inherited in a Mendelian fashion. In some subsets of patients there is a particularly high rate of occurrence of unusual alleles. . . These results suggest that (a) particular Ha-ras alleles may be associated with increased risk for certain cancers; (b) Ha-ras may play a more prominent role in tumorigenesis than previously suspected; and (c) such a role is not tissue specific. We have now begun to characterize molecular clones of several rare alleles from myelodysplasia and melanoma to determine if germ line abnormalities of the Ha-ras gene may be detected.

Case control analysis of neuroblastoma and paternal occupation. M.R. Spitz, C.C. Johnson, G.R. Newell, M.D. Anderson Hospital & Tumor Institute.

The peak incidence of neuroblastoma (NBL) during early infancy suggests that prezygotic or prenatal exposures to carcinogens could be implicated. Several recent epidemiologic studies have noted an association between parental exposure to hydrocarbons and the aircraft manufacturing industry and the development of nervous system cancer in the offspring. This is a case control epidemiologic study of paternal occupation of 157 children under 15 years of age who died from NBL in Texas during 1964-1978. As controls, 314 children were selected by stratified random sampling from all Texas live berths with the same birth year distribution as the cases... Neither hydrocarbon related work exposure nor employment in the aircraft industry was associated with increased risk for NBL. However, we demonstrated that children of fathers employed in occupations with electromagnetic field exposure were at significantly increased risk for NBL (odds ratio = 2.14). These occupations included electricians, electric and electronics workers, linemen, and utility employees and welders. The odds ratio was 11.3 for children of fathers who reported themselves to be electronics workers (6 cases, 1 control).

Genetic studies of hereditary melanoma (HM) and its precursor, the dysplastic syndrome (DNS). M.H. Greene, S.J. Bale, A. Chakravarti, D.L. Mann, C. Murray, A.H. Johnson, D. Gerhard, D.E. Housman, NCI, Univ. of Pittsburgh, Uniformed Services Univ. of Health Sciences, Georgetown Univ., MIT.

Based upon a detailed clinical/lab assessment of 401 members of 14 HM/DNS prone kindreds, we reported that this condition appears to be inherited as an autosomal dominant disorder and that an HM/DNS susceptibility gene may be located on the short arm of chromosome 1 (PNAS 80:6071, 1983). Additional genetic analysis of these families, using life table techniques, has now provided further support for autosomal dominant inheritance: the estimated segregation ratios for HM (0.47) and DNS (0.54) are not significantly different from the ratio predicted by a dominant model (0.50). . . This. . . provides the first evidence that HM and DNS represent pleiotropic effects of a single highly penetrant gene. . . This project has clarified the etiology of HM and provided new approaches to the prevention and control of malignant melanoma.

Genetic epidemiology of childhood soft tissue sarcoma (STS). W.R. Williams, L.C. Strong, T.L. Norsted, M.D. Anderson Hospital & Tumor Institute.

In 1969 Li and Fraumeni described a familial aggregation of childhood STS, breast cancer and other neoplasms. To determine the frequency and etiology of this syndrome, we identified a cohort of 3 year survivors of childhood STS from M.D. Anderson. . . Of 163 eligible patients, 159 were informative and participated in the study. There were 2,451 relatives at risk identified, 197 with confirmed cancer. Multifactorial heritability of 0.13 revealed a small but significant degree of familial cancer aggregation ($P<.01$). . . Contrasts of sporadic, multifactorial and dominant gene models for each kindred revealed that 11 kindreds accounted for most of the familial aggregation, and the cancer pattern favored a dominant gene in nine of those kindreds. Excess of soft tissue, bone, breast, cervix, brain, prostate, melanoma and stomach cancer were observed in those kindreds. Overall, 6-7% of families of STS survivors may be at high risk of various cancers due to a rare autosomal dominant gene.

Complete tumor ablation with iodine 131 radiolabeled monoclonal antibody (MoAb) against human neuroblastoma (NB) xenografted in nude mice. K.V. Cheung, B. Landmeier, S. Kallick, D. Nelson, S. Ellery, R. Adams, J. Neely, P. Coccia, F. Miraldi, Case Western Reserve Univ., Rainbow Babies & Childrens Hospital and Univ. Hospitals of Cleveland Clinic.

The antibody 3F8, an IgG3 murine MoAb we have developed to human NB, could specifically target iodine 131 to human NB xenograft with tumor to non tumor ratios of 10-100 and a relative radiation dose deposition to normal organs of 1 to 20% of that to the tumor. We therefore studied its efficacy in tumor therapy. Nude mice with actively growing sc

human NB (1-2 gm size) were injected with 0.125 to 1 mCi iodine carried on 100-200 ug MoAb 3F8. Tumor size was followed by direct measurement... Tumor shrinkage only occurred with 131-I 3F8 MoAb, but not with nonradioactive 3F8 or radiolabeled irrelevant MoAb. While control mice tumor enlarged by 10 fold, treated tumor showed >95% shrinkage by 12 days. Both the rate of shrinkage and duration of response were dose dependent. Only those tumors that received >4700 rads were completely ablated without recurrence. Recurrent tumors were successfully reimaged with 3F8 and responded to a second 131-I MoAb treatment. There were no toxicities except reversible weight loss. No gross abnormalities were found in organs. These results confirmed our prediction based on our imaging studies that human NB xenografts could be effectively eradicated using iodine 131 labeled MoAb 3F8 with tolerable toxicities.

Epidermal growth factor binding is increased in multidrug resistant cells. Marian Meyers, Barbara Spengler, June Biedler, Memorial Sloan-Kettering Cancer Center.

Human neuroblastoma, Chinese hamster lung and mouse tumor cells, selected for resistance to vincristine or actinomycin D and cross resistant to a wide variety of agents such as daunorubicin and adriamycin, have increased levels of (125-I) epidermal growth factor (EGF) binding, ranging from 1.5 to seven fold, as compared to their respective parental cells. Affinity labeling studies with that ligand show that increased binding corresponds to increased amounts of EGF receptor protein. The EGF receptor complex was visualized by radioautography of sodium dodecyl sulfate polyacrylamide gels as a species with molecular weight of about 170 KD... Human epidermoid A431 cells with unusually high EGF receptor content were found to be equally or more sensitive to vincristine and actinomycin D when compared to other human and rodent cell lines. Thus, cells with high levels of EGF receptor are not intrinsically multidrug resistant. Increase in receptor level may be a necessary consequence of resistance development and suggests an increased dependence on EGF for cell growth. Receptor increase, therefore, may be associated with the reverse transformed phenotype (reduced tumorigenic potential and change toward normal cell morphology and growth behavior in culture) exhibited by these multidrug resistant cells.

Detection of pleiotropic drug resistance (PDR) by immunofluorescent assay of drug effects on cytoskeleton. H. Mujagic, E. Hamel, G. Curt and B.A. Chabner, NCI.

We have developed a method for detecting PDR by observing the effects of vincristine on the microtubular system in tumor cells in culture. Drug sensitive MCF-7 human breast cancer cells and three mutants developed by incubation with serially increased concentrations of colchicine were studied. The PDR mutants exhibited resistance to adriamycin, vincristine, and vinblastine, as well as to colchicine; their tubulin content, the affinity of tubulin for colchicine, and the number of binding sites of colchicine per mg protein were the same as in sensitive cells. However, with immunofluorescent staining of the microtubular network, the PDR cells lacked distinct microtubule organizing centers and paracortical microtubules. Upon exposure to 0.03/uM colchicine, sensitive MCF-7 cells exhibited a loss of the organizing center and the filamentous microtubular network within 3 hours and developed deposits of paracrystals of tubulin. The microtubule staining pattern of PDR cells was unaffected by colchicine. If after incubation with colchicine for up to six hours the drug sensitive MCF-7 cells were resuspended in drug free medium, the microtubular system was again detected in a minority of cells after eight hours and was completely reformed after 20 hours. This method of immunofluorescent staining of the microtubular apparatus offers the potential of recognizing cells resistant to tubulin binding agents, and may furthermore be useful for detection of the PDR phenotype in clinical tumor samples.

Monoclonal antibodies to glycoproteins associated with multiple drug resistance (MDR). Mary Danks, Dennis Metzger, Richard Ashmun, William Beck, St. Jude Children's Research Hospital.

Tumor cell resistance (R) to one "natural product" anticancer drug is often associated with cross-R to other drugs and is termed MDR. We have shown that human leukemic cells (CEM) selected for R to vinblastine (CEM/VLB100) express MDR and are characterized by changes in cellular pharmacology and surface glycoproteins (gps). Most prominent is the enhanced expression of a high molecular weight gp of 180,000 daltons, the amount of which is related to the degree of R. We report here the production of three MoAbs that bind preferentially to the surface of CEM/VLB100 cells as determined by indirect fluorescence microscopy and flow cytometry. Some cell lines of intermediate resistance to VLB show intermediate levels of fluorescence. Each antibody recognizes a surface membrane gp of about 180 kd as determined by immunoprecipitation of surface or metabolically labeled cells. Studies with tunicamycin, an inhibitor of protein glycosylation, suggest that MoAb 32G7 recognizes the carbohydrate moiety of gp180. Two of the MoAbs also recognize a second surface gp of either 155 kd or 130 kd. All of these gps are overexpressed in CEM/VLB100 cells... CEM cells selected for R to vincristine, doxorubicin, VM-26 or methotrexate also have varying amounts of gp180. These MoAbs may be useful in studies of

the mechanisms of MDR, as well as in determining whether cells from drug resistant patients bear these resistance associated gps.

Comparative activity and toxicity of adriamycin (ADM) and new anthracycline analogs in advanced breast cancer. V. Bonfante, A. Rossi, C. Brambilla, L. Ferrari, F. Fillani, R. Comazzi, F. Crippa, S. Monfardini and G. Bonadonna, Istituto Nazionale Tumori.

A randomized study with ADM vs. 4'epi-ADM (epi-ADM) and three phase 2 oriented studies with 4'deoxy-ADM (dx-ADM) and with 4 demethoxy-daunorubicin (dm-DNR), given intravenously and orally (po), were performed in patients with advanced breast cancer not pretreated with anthracyclines. Cardiac toxicity was evaluated by serial determinations of left ventricular systolic time intervals (PEP/LVET), a minor axis shortening (MAS) and left ventricular ejection fraction (LVEF). Comparative results are reported below; the variations of cardiac parameters are those recorded at the end of drug treatment over basal values.

	ADM	epi-ADM	dx-ADM	dm-DNR iv	dm-DNR po
mg/m^2 q. 3 wks	75	75	35	13	45
Med. Cumul. Dose	540	565	175	52	180
Eval/Total	21/22	21/25	24/25	22/28	19/26
CR + PR	52	62	21	14	26
Vomiting (%)	72	53	29	32	72
Alopecia (%)	100	100	46	5	33
WBC < 4,000/mm^3 (%)	51	19	25	36	55
↑ > 15% PEP/LVET (%)	55	18	33	14	40
↓ > 15% MAS (%)	31	11	17	22	17
↓ > 15% LVEF (%)	31	12	14	0	0

Clinical symptoms and signs of cardiac damage were observed only in two patients treated with ADM after cumulative dose of 562 and 580 mg/m2. When given at the same dose, epi-ADM was equally effective as ADM but induced less vomiting, myelosuppression and cardiac toxicity. At the dose schedule employed, dx-ADM and dm-DNR resulted less toxic but definitely less active in advanced breast cancer.

Update of cyclic chemotherapy in 100 patients with advanced nonseminomatous germ cell tumors (NSGCT). C. Logothetis, M. Samuels, D. Selig and F. Dexeus, M.D. Anderson Hospital & Tumor Institute.

CISCA-11/VB-IV (cytoxan 500 mg/m2 x 2, adriamycin 45 mg/m2 x 2, cisplatin 120 mg/m2 x 1 / vinblastine 3 mg/m2 x 5, plus simultaneous bleomycin 30 mg x 5) cyclic chemotherapy was delivered in 100 patients with NSGCT (91 testis primary, 9 extragonadal). An overall 91% continuous disease free survival was achieved (92% testis primary, 56% extragonadal primary). Thirty two patients required surgical exploration for a stable postchemotherapy mass. All 32 patients are alive and NED with no viable cancer at surgery. Only 2% achieving a complete response have relapsed (mean followup 132 weeks, median 126 weeks). Eleven patients failed to achieve a durable CR: one died of chemotherapy toxicity... Acute toxicity was severe. . . One patient died of toxicity, one patient developed nonfatal bleomycin pulmonary toxicity, and two patients had a transient >10% drop in ejection fraction. Cyclic chemotherapy continues to achieve superior results to PVB chemotherapy resulting in a higher continuous disease free state, a reduced response rate and a reduction in long term toxicity.

CANCER LETTER ADDS ASSOCIATE EDITOR

Patricia Williams, who has been reporting on NCI and NIH for the "Blue Sheet," has joined the staff of **The Cancer Letter** as associate editor. She is a graduate of the Univ. of Missouri School of Journalism.

Williams will assist on NCI coverage, including the National Cancer Advisory Board and President's Cancer Panel, as well as with the various professional societies.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-5772548
Title: Support services for extramural clinical trials
Deadline: Approximately Sept. 24

The Cancer Therapy Evaluation Program of the Div. of Cancer Treatment is seeking an organization with the capabilities and facilities to provide support for its management of the extramural clinical trials program. Two major categories of support are required: (a) Direct organizational data management and statistical support for specific clinical trials; (b) Information management assistance to the CTEP professional staff in the analysis of methodology and data emanating from the extramural program.

Offerors will be required to demonstrate in their technical proposal in a separate section entitled "Mandatory Qualification Criteria for the Performance of the Project" how it will satisfy the following requirements of this project:

A. Daily access by the contractor to printed material maintained by CTEP staff in several locations in the Landow Bldg in Bethesda.

B. NCI staff will require frequent access (as often as weekly) to the hard copy data files maintained and analyzed at the offeror's facilities, and frequent contact (as often as weekly) with the

project director to discuss technical problems and to review data.

Failure to demonstrate these capabilities will result in the offeror's elimination from further consideration.

The government anticipates that one contract will be awarded on an incrementally funded basis for 60 months.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in The Cancer Letter Nov. 2, 1984, page 8.

Contract Specialist: Thompkins Weaver
RCB Blair Bldg Rm 228
301-427-8737

RFP NCI-CM-5772148
Title: Cancer Therapy Evaluation Program information system

Deadline: Approximately Sept. 24

The Cancer Therapy Evaluation Program is seeking an organization with the capabilities and facilities to design, develop and implement an integrated data management system to merge the current separate CTEP information systems i.e, the CTEP Information System (CTEPIS) and the Drug Distribution and Protocol Monitoring System (DDPMS). Offerors are to make recommendations to the ultimate hardware and software to be utilized by the merged system. The merged system will be owned by the government. However, the contractor will maintain the system, and it will remain in the contractor's possession as long as the contract is in effect. All data rights, patents, and copyrights will be retained by the government. Offerors will be required to demonstrate in their technical proposal how they will accomplish the task of attendance at daily meetings with NCI personnel in Bethesda.

The government anticipates that one contract will be awarded on an incrementally funded basis for a period of 57 months.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in The Cancer Letter Nov. 2, 1984. all and reported in The Cancer Letter Nov. 2,

Contract Specialist: Thomkins Weaver
RCB Blair Bldg Rm 228
301-427-8737

NCI CONTRACT AWARDS

TITLE: Assay development and preclinical pharmacology studies with anthrapyrazole (NSC-349174), task #12
CONTRACTOR: Mayo Foundation, $60,043.

TITLE: Assay development and preclinical pharmacology studies with diazohydroxide (NSC-361456D), task 13
CONTRACTOR: Mayo Foundation, $81,674.

TITLE: Methodology and analysis of vitamin A and carotenoids in foods
CONTRACTOR: Arthur D. Little, Inc., Cambridge, Mass., $1,048,756.

TITLE: Resource for xenotransplantation and evaluation of human tissues and cells in athymic nude mice
CONTRACTOR: Litton Bionetics Inc., $1,308,961.

TITLE: Prenatal x-ray exposure and childhood cancer in twins
CONTRACTOR: National Institute of Environmental Medicine, Stockholm, Sweden, $146,844.

TITLE: Bovine leukemia herd
CONTRACTOR: Univ. of Pennsylvania, $379,459.

TITLE: Record linkage studies utilizing resources in population-based tumor registries
CONTRACTOR: Institute of Oncology in Ljubljana, Yugoslavia, master agreement.

TITLE: Biomedical computing software services in support of the Diagnostic Program
CONTRACTOR: Information Management Services, Inc., $743,660.

TITLE: Support for Cancer Surveillance System, Cancer Epidemiology & End Results (SEER)
CONTRACTOR: Northern California Cancer Program, $6,709,330.

Title: Thyroid cancer risk following diagnostic and therapeutic 131-I exposure
Contractor: Karolinska Institute, $412,978
Title: Epidemiologic survey of leukemia/lymphoma for leukemia/lymphoma virus
Contractor: Medicala Research Council, $848,985

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House Committee on Appropriations
Subcommittee on Labor-HHS-Education
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The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams

Published forty-eight times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.