THE CANCER LETTER

Vol. 12 No. 41
Oct. 24, 1986

Subscription $160 year North America
$175 year elsewhere

P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

CGOP Gets Concept Approval; DCT Releases RFAs For Lung, Colon Drug Discovery Groups

The Cooperative Group Outreach Program, transferred earlier this year from the Div. of Cancer Prevention & Control where its fate was highly uncertain, received

(Continued to page 2)

In Brief

Congress Finishes Spending Bill, Reagan Signs It; NCI Gets $1.402 Billion, A $174.5 Million Raise

CONGRESS FINALLY wrapped up the massive spending bill which funds all government agencies for the rest of the 1987 fiscal year last week and promptly went home to get in some last minute campaigning. They left behind some happy folks at NCI: Appropriations for the Cancer Program represents the largest single year increase since the early days of the National Cancer Act. As reported last week, Congress accepted the conference report on the regular Labor-HHS-Education appropriations bill, which included $1.402 billion for NCI. That's one billion, 402 million, 837,000 dollars--$174.5 million more than NCI received in FY 1986. NIH received $6.18 billion along with the mandate to fund 6,200 new and competing renewal grants. The NCI total includes $61 million for AIDS research; the NIH total, $247 million. President Reagan signed the measure, which included a combination of a few budget cuts and revenue increases to make it appear for now, at least, that Gramm-Rudman-Hollings across the board cuts will not be necessary. . . . **JOHN KILLEN**, deputy chief of the Clinical Investigations Branch of NCI's Div. of Cancer Treatment, has left the government to become medical director of Whitman-Walker Clinic in Washington DC. The clinic is a major provider of AIDS services and support programs, including complete medical care for AIDS patients and persons testing positive for the HTLV-3 virus. Killen was with NCI for six years. . . . **OTHER DCT** staff changes: **Leslie Friel** is the new administrative officer of CTEP, replacing Don Poppke; **Betsy Duane** has replaced Barbara Vermillion as acting AO for the Radiation Research Program. . . . **JAMES NEIDHART**, medical director of the Univ. of New Mexico Cancer Center, has been appointed interim director of the center, with the departure of **Thomas Tomasi**, now director of Roswell Park Memorial Institute. Tomasi also was chairman of the UNM Dept. of Cell Biology; new interim chairman is **Nicholas Matwiyoff**, who is director of the UNM Center for Non-Invasive Diagnosis.

CGOPs To Be Reviewed For Renewal When Parent Groups Are Reviewed

(Continued from page 1)
concept approval from the Div. of Cancer Treatment Board of Scientific Counselors last week and now appears to be a permanent fixture on the clinical trials scene, or at least as permanent as any program supported by NCI can be.

In another major development, DCT released two new RFAs (technically, "revisions" of an old one, so termed to avoid bureaucratic hangups at NIH headquarters), for national cooperative drug discovery groups for lung and colon cancer. Plans for the new groups, patterned after the four existing drug discovery groups which are not disease oriented, were presented to the DCT Board last winter (**The Cancer Letter**, Feb. 21). At that time, DCT Director Bruce Chabner said he was not asking for concept approval because he didn't think the money would be available to fund them in FY 1987.

But the NCI Executive Committee later decided that searching for new lung and colon cancer therapies were high priority items, and the money (an estimated $3 million the first year) was earmarked. The DCT Board gave concept approval by mail. The final hurdle--NIH has to approve all RFAs and use of the cooperative agreement mechanism--was cleared when DCT's Developmental Therapeutics Program convinced the brass that this was merely a revision of the previous RFA for non-disease oriented groups.

CGOPs Vital To Trials

Only a few months ago, CGOP was close to elimination. Neither DCPC Director Peter Greenwald nor his Board of Scientific Counselors felt the program belonged in that division. It was started in 1976 as a cancer control effort, to improve quality of care in community hospitals by making clinical trials available to patients there. As the program matured, the participating community hospitals became accepted on the same basis as the university hospitals. DCPC argued that it was an integral part of the cooperative groups and that it should be managed, and funded, by the division which has the cooperative groups--DCT.

DCT didn't argue with that but insisted it did not have the money, $4 million a year, to support the program (**The Cancer Letter**, July 25). DeVita managed to find the money and the transfer was accomplished. However, the program's concept approval was due to expire in 1987, and DCT sought concept approval for five more years.

Board members agreed that the program should be continued but decided that rather than approve a recompetition for five years, the CGOPs of each of the seven cooperative groups in the program should be reviewed at the same time their parental group is reviewed. Those are generally reviewed every five years, with four or five groups being reviewed each year.

The seven participating cooperative groups have come to rely heavily on their CGOP affiliates for patient accrual. In the staff statement justifying continuation of the program, the Cancer Therapy Evaluation Program, which is responsible for the cooperative groups, said, "Adequate patient accrual to these high priority studies remains a challenging problem for the investigators and for NCI."

CTEP noted that CGOP "has evolved to include the following objectives:

*Making state of the art cancer management available to cancer patients treated in the community.

*Enhancing recruitment of patients in community hospitals onto appropriate protocol studies.

*Involvement of a wider segment of the community in clinical research activities through a network of communicating physicians or hospitals.

*Evaluation of these concepts and efforts.

CTEP said the $4 million budget was largely committed for the personnel required to implement the program objectives at the community level. "This program has constituted a very effective supplemental mechanism for the recruitment of patients onto clinical research protocols of national importance at the community level. Over 4,000 patients were added to clinical trials through this mechanism in the past year alone, which was one sixth of the total patient accruals in the enter Cooperative Group Program, at a cost which is about one sixteenth of that Program. The demonstrated high quality of the data derived from these patients has made them a vital resource within the Cooperative Group Program."

The suggestion had been made, when it looked as if CGOP was on its way out, that it was no longer needed now that the Community Clinical Oncology Program was in operation and appeared to be successful. But CCOPs

are larger hospitals or consortia of hospitals, clinics, and other entitities because they play a larger management role in their clinical research efforts. CCOPs and CGOPs both work with cooperative groups, using group approved protocols, but CGOPs rely more on the groups for the management activities. Also, CCOPs have a large patient accrual requirement, while a smaller CGOP sometimes enters only a handfull of patients each year.

CGOP experience has helped build cancer programs in the smaller hospitals. Many of them competed successfully for a CCOP award in the first round, and even more are involved in the current recompetition.

Targeted Drug Development

The Developmental Therapeutics Program hopes to support four lung cancer and two colon cancer National Cooperative Drug Discovery Groups at an estimated annual total cost of about $500,000 each. RFA 87-CA-01, for the lung cancer groups, includes a set aside of $2 million for the initial year's funding, while RFA-87-CA-02 has set aside $1 million.

John Venditti is program director for the National Cooperative Drug Discovery Groups in DTP. His summary description of the colon and lung RFAs states that the "programs are designed to assist leading researchers in diverse scientific disciplines to interact as a unit, regardless of their individual instituional affiliations or prior direct involvement in cancer related research. The purpose is to mobilize, with NCI support, the outstanding talents required to exploit leads from fundamental studies and to extrapolate them to improved treatments for these high incidence malignancies. Each (lung or cancer group) is envisioned as being composed of a principal investigator and a number of program leaders who will conduct interdependent and synergistic laboratory programs to conceptualize, create, and evaluate preclinically new therapies in accordance with the applicant's scientific goals and technical approaches to goal achievement. A group may be made up of scientists in academic, nonprofit research, and commercial organizations."

Venditti emphasized that the "active participation of industry is encouraged, because it will allow this segment of the scientific community to contribute its considerable intellectual and material resources. The interaction of academic and research organizations with industry and government will facilitate subsequent development (preferably through private venture capital, but alternatively, by government) and marketing of new inventions."

Copies of the complete RFAs and further information may be obtained from Dr. John Venditti, Landow Bldg Rm 5C08, DCT, NCI, Bethesda, MD 20892, phone 301-496-8783.

NCI's Drug Development Program, managed by DTP, has been continually cut back in recent years as the result of budget and personnel reductions.

DTP Director Michael Boyd told the Board that 22 sections from his branches have been eliminated or consolidated. The budget for drug development has dropped from $33.3 million in 1982 to $26.1 million in 1986.

Nevertheless, Boyd said that during the 1987 fiscal year, DTP will continue to develop and apply new screening systems, carry on with the search for new natural and synthetic agents with anticancer potential and emphasize development of the national drug discovery groups.

DTP is in the process of implementing a major change in drug screening. About two years ago, a program was initiated of testing candidate compounds against human tumor cells in vitro. It was run in parallel with the established P388 mouse screen, with the results to be evaluated. If the in vitro screen proved to be as effective as the P388, the animal prescreen would be dropped.

NCI Director Vincent DeVita told the National Cancer Advisory Board earlier this month that a decision was near on dropping the P388 prescreen, "although some people feel this would be a mistake."

When NCAB member Enrico Mihich asked that if the prescreen is done entirely in vitro whether compounds with activity there would be tested in animals, DeVita replied that they would. "We can't do without animals entirely.

"I'm rather amazed at the job that's been done," DeVita continued. "We've seen in vitro attempts for 20 years, but this is the first time that it's worked. We're very pleased with Mike Boyd's work."

The DCT Board will hear a complete evaluation of the in vitro screen at its February meeting, at which time it may be asked to approve the changeover.

Other concepts approved by the Board last week were:

Iso-antigenic typing of mouse strain. Recompetition of a contract held by Northestern Univ. which will total almost $600 million over five years, ending in 1987. The recompetition will be for five years, kwith an estimated first year award of $140,000.

This contract performs skin grafts which provide assurance that inbred strains remain histocompatible with NIH maintained foundation colonies. Major histocompatibility problems are identified within 30 days by this system, but grafts are held for 100 days in order to identify minor problems. The major advantage of this approach to histocompatibility testing is that subtle problems such as mutations (genetic drift) can be identified only through skin grafting.

Each year this contract receives approximately one percent of the breeders from each foundation, pedigreed expansion, and production colony within the total program. At the same time, depending on availability, animals of the same strain are sent to the contractor from the NIH repository and used as reference animals. The animals from production contractors are tail grafted onto NIH reference animals and vice versa. In addition, within line grafts are done on each source of animals supplied. All of these animals are shipped according to a schedule drawn up by the project officer.

During the past three years this contract has identified several strains of mice with minor compatibility problems, probably due to genetic drift. This identification enabled the staff to make adjustments before a problem became significant.

Boyd said that much of the cost of the contract is recovered through reimbursement from users of the animals.

Maintenance of a rodent production center. The current program involves four contracts, with Charles River Laboratory, Harlan Sprague Dawley, Simonsen Laboratory, and Taconic Farms, at a total combined cost of about $650,000 a year in FY 1986. The recom- petition will be just for one contract, for the production of nude mice, with an estimated cost of $180,000 the first year of a three year award.

These contracts have been responsible for producing large numbers of CD2F1 hybrids for the DTP screening program. Since the screening program is being substantially cut back, three of the four will not be funded in FY 1987--Charles River, Harlan Sprague Dawley and Simonsen. The hybrid offspring are sent weekly to the DTP screening contractors, NIH on campus investigators and to NIH grantees.

Taconic Farms will continue to produce athymic nude mice in 1987. This has been at a level of 3,000 female breeders, which are sent weekly to the same consignees as for the hybrids, as instructed by NCI. In total, the four contracts produced about 6,000 hybrid mice and 1,500 athymic mice per week.

The continued production of nude mice will be dependent on the need for them at the time and on what production adjustments can be made in the primary genetic center contracts. This effort (as with all animal production contracts) will be modified or eliminated as usage requirements dictate changes.

Biochemical genetic monitoring of rodents. Recompetition of a contract held by Texas A&M Univ. which has increased from $44,500 in FY 1983 to an estimated $65,000 in FY 1987. Estimated first year cost of a five year award, to start in January, 1988, is $70,000.

This contract utilizes biochemical markers (isozymes) to monitor the genetic integrity of inbred and first generation hybrid rodent strains. This contract serves a very useful purpose in that breeding errors (most likely source of genetic contamination) will be identified very quickly because of the short time frame for testing (less than one week). Consequently, corrective measures can be investigated before major problems occur.

This contract receives 10 mice per week from each of two inbred strains. The mice are checked for 11 critical biochemical markers that are specific for the strain. Throughout the period of one year all foundation, pedigreed expansions, and production colonies are checked.

It was a result of this contract that genetic contamination and/or drift was detected in three inbred strains.

Clinical trials monitoring service. Recompetition of a contract held by Theradex, which will cost an estimated $1.3 million in FY 1987, the last year of a five year contract. The recompetition will also be for five years, with an estimated first year cost of $1.375 million.

The Clinical Trials Monitoring Service has four functions: (1) central data management resource for phase 1 and certain phase 2 studies; (2) periodic monitoring site visits of early phase 1/2 studies as required by FDA regulations; (3) co-site visiting 10-20% of cooperative group audits of their members, to assure compliance with NCI, NIH and FDA policies and regulations; and (4) site visit monitoring of all other investigators and institutions conducting trials with DCT sponsored investigational agents at least once every three years.

Because the contractor has been assigned to provide central data management and to site visit monitor the LAK-IL-2 studies initiated over the past year and

- -

CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY; RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) or RFAs (grants and cooperative agreements). Availability of the RFPs and RFAs will be announced when the Institute is ready to release them.

- -

planned for the future, the use of the level of effort of the current contract has been accelerated. DCT now expects the current contract to be completed by Dec. 1, 1987, rather than June 30, 1988.

During the past three years, a total of 47 monitoring site visits to 36 single institutions conducting research with DCT sponsored investigational drugs have been completed. All major extramural cancer centers have been audited. The findings from these audits have led to productive discussions among CTEP staff, NCI cancer center program staff, and center directors about ways to improve the conduct of clinical trials in the cancer center setting.

Data on 243 phase 1 or 2 studies have been collected, and monthly reports produced for CTEP and the investigators. Monitoring site visits were conducted three times a year at the institutions conducting these phase 1 or 2 studies (25-35 institutions at any given time). A standard case report form has been developed for use in all monitored studies, and remote data entry has been established for all phase 1 contractors. Contractor staff attended an average of 35 cooperative group site visits each year.

Future plans include continued data monitoring of phase 1 and selected phase 2 trials of cytotoxic drugs

and biologic response modifiers; site visit monitoring of the same studies; and assisting DCT in site visit monitoring of cooperative groups and other investigators and institutions engaged in DCT sponsored investigational drug studies.

A central data base of patient information for phase 1 cytotoxic and BRMP studies and selected phase 2 studies will be maintained. This aspect will require about $820,000 per year.

These same satudies will be monitored through data audits conducted three times each year (70/year average). These audits require approximately $136,500.

Co-site visiting about 10-20% of cooperative group institutions (25/year average) requires about $136,500 per year.

Planning, organizing and conducting monitoring site visits to other institutions (15/year average) requires approximately $282,000 per year.

AIDS update New Supplement For Subscribers of Cancer Letter

This issue of **The Cancer Letter** includes the supplement, **AIDS update**, the second monthly supplement which will be distributed to subscribers along with their regular issues of the newsletter. **Cancer Economics**, which went out with last week's issue, is the other.

With AIDS fast becoming one of the country's most urgent public health problems, the federal government has responded with increasingly greater commitments of its health research and services resources. The budget for AIDS research at the National Institutes of Health in the 1987 fiscal year will be $247 million. Most of that will be awarded in contracts, grants and cooperative agreements to investigators around the U.S. and abroad.

Nearly all of the AIDS related contracts and cooperative agreements will be the result of initiatives developed in policy discussions among NIH staff and a variety of nongovernment advisors. Decisions coming out of those discussions, and other actions of NIH, Food & Drug Administration and other federal agencies, are occurring almost daily.

The Cancer Letter began reporting on AIDS research activities as soon as NCI and NIH became involved. Cancer investigators joined their colleagues in other NIH institutes in the pioneer studies, and practicing oncologists have been heavily involved in managment of AIDS patients. **The Cancer Letter** will continue to report urgent AIDS developments in its regular weekly issues. **AIDS update** will provide a monthly report of news and actions from the agencies involved. Reports will include coverage of policy development and discussions, so the scientific community may follow and participate in those decisions and be ready to quickly respond when the RFAs and RFPs are issued.

Two AIDS related RFAs have been released by the National Institute of Allergy & Infectious Diseases. Summaries, and information on announcements by the Alcohol, Drug Abuse & Mental Health Administration follow:

RFA 87-AI-01

Title: Biological and biophysical properties of HTLV-3/LAV and related retroviruses
Application receipt date: Jan. 5, 1987

The National Institute of Allergy & Infectious Diseases invites applications for regular research grants to investigate the biological and biophysical characteristics of HTLV-3/LAV. Investigators may propose studies to investigate the biological, biophysical, biochemical or structural properties of this virus or any of its components. Proposals to focus on one or more of these areas of investigation are encouraged. Applications involving other collaborating scientists or institutions are encouraged, but not required for response to this announcement. Included in the scope of this announcement is the study of the relationship between structure and function of any of the components of HTLV-3/LAV or related retroviruses.

Investigators are encouraged to consider projects to determine the three dimensional structure of envelope glycoproteins, reverse transcriptase, gag protein, or other viral components and to relate structural studies with biological, biochemical or biophysical processes. Studies to identify biological or biochemical mechanisms of viral penetration into susceptible host cells, release of viral particles from infected cells, regulation of biochemical events involved in the replication of these viruses or the regulation of the latent state are particularly encouraged.

NIAID expects to allocate $2.5 million to specifically fund applications in response to this RFA. The number of awards to be made is dependent upon receipt of a sufficient number of applications of high scientific merit and upon the availability of funds. The earliest possible award date is July 1, 1987.

Additional information and copies of the complete RFA may be obtained from Chief, Pathogeneis Branch AIDS Program, NIAID, NIH, Westwood Bldg Rm 753, Bethesda, MD 20892, phone 301-496-0545.

RFA 87-AI-02

Title: Immunopathogenesis of HTLV-3/LAV infections
Application receipt date: Jan. 5, 1987

NIAID invites applications for regular research grants to investigate the pathogenesis of HTLV-3/LAV/HIV. These studies can explore any of the components of the immune system, cellular or humoral, as well as properties of the virus or host that are responsible for or contribute to pathologic processes encountered in this infection. Animal model systems may also be investigated.

The central feature of AIDS infection is that it is an infection of the immune system, specifically the T-helper cell. Accordingly, the infected host becomes susceptible to a variety of opportunistic infections and to various malignancies. Moreover, the virus has the capability to establish a latent state in the cells of the immune system. Many factors have been postulated that may play a role in the pathogenesis of this infection. These may include processes mediated by the virus itself, the immune system or other

factors. It is important to understand the pathogenic processes in order to develop methods to control or prevent these effects.

Since this is an infection of the immune system it is likely that processes mediated by immunologic mechanisms are involved in the pathogenesis of this infection. In addition, the virus may have other important features that are important in the pathogenesis of this disease, such as neurotropism. Accordingly, NIAID wishes to solicit regular research grant applications in this general area of pathogenesis to determine if other properties of the virus or of the host's response to infection can explain the pathologic processes that occur during or as a result of this infection.

NIAID expects to allocate $2.5 million to specifically fund applications in response to this RFA. Earliest possible award date is July 1, 1987.

Additional information and copies of the complete RFA may be obtained from the chief of the Pathogenesis Branch, AIDS Program, address and phone number as shown with the RFA above.

MH-86-16: Revision

Title: AIDS research centers
Application receipt dates: Nov. 1, 1986, and March 15, 1987

The Alcohol, Drug Abuse & Mental Health Administration has revised its announcement on AIDS research centers. The statement concerning a maximum amount of $500,000 (direct costs) per year has been eliminated. In addition, the award criteria now read as follows: quality of the proposed center as determined during the review process; availability of funds; program balance; geographic distribution; and emphasis on both mental health and drug abuse aspects.

Further information may be obtained from Dr. Fred Altman, National Institute of Mental Health, 5600 Fishers Lane, Rockville, MD 20857, phone 301-443-4337.

NCI CONTRACT AWARDS

Title: Record linkage study of occupation and cancer
Contractor: Shanghai Cancer Institute, $47,784

Title: Continuation of followup on participants in the Breast Cancer Detection Demonstration Project
Contractor: Westat Inc., $2,766,886

Title: Feasibility study of radiation workers with individual dosimetry determinations
Contractor: R.S. Landauer Co., $86,022

Title: Support services for clinical epidemiologic studies
Contractor: Westat Inc., $1,479,541

Title: Synthesis of compounds by small business for preclinical toxicology and phase 1 clinical studies
Contractor: Starks Associates Inc., $1,121,967

Title: Tracing through other sources for telephone followup of X-ray technologists not responding to a questionnaire
Contractor: Johns Holding Co., $103,250

Title: Synthesis of compounds for preclinical toxicology and phase 1 clinical studies
Contractor: Aldrich Chemical Co. Inc., $1,227,210

Title: Epidemiology and treatment of human T-cell leukemia/lymphoma virus in Jamaica
Contractor: Univ. of The West Indies, $904,355

Title: Human tumor cell bank
Contractor: American Type Culture, $1,392,110

Hepatitis A Source in LAK-IL-2 Study Found; Six Patients Suffer MIs

The search for the source of the hepatitis A contamination which has caused the six extramural clinical studies of lymphokine activated killer cells-interleukin-2 therapy to be suspended has been narrowed to the company that supplied sera in which the cells are cultivated, Div. of Cancer Treatment Director Bruce Chabner told the division's Board of Scientific Counselors last week.

The trials in the six institutions, initiated as confirmatory studies of the regimen developed by NCI's Steven Rosenberg, were suspended in late August when hepatitis A manifested itself in significantly large numbers of the patients receiving LAK-IL-2.

Chabner said that "we are trying to find an alternative source for the sera. So far, it's all been from one company. It is very unusual. Also, we're trying to develop a serum free method of cultivating cells."

Maryanne Roper, special assistant to NCI Director Vincent DeVita, reported that an important new toxicity, myocardial infarction, had appeared in three patients in the extramural trials. One of three died. Three patients in Rosenberg's intramural studies also had MIs.

Roper said there were 15 grade 4 toxicities in the extramural studies, including the MIs, coma and pulmonary complications. All were totally reversible.

Before the studies were suspended, 94 patients had been accrued. Thirty four patients with renal cell cancer were treated, 30 are evaluable, with one complete response and three partial responses (50% or more shrinkage of tumor). There were 29 evaluable melanoma patients, with five partial responses; 17 colon cancer patients, with two partial responses; and one non-Hodgkins lymphoma patient, who had a partial response. Of 94 patients, 77 are evaluable, with one complete and 11 partial responses, Roper said.

"With the hepatitis problem, we have time to ponder where we will go from here," Roper said. "We're trying to decide, when we resume the studies, whether we should focus on renal cell cancer and melanoma. We are looking at modifications to increase the efficacy and are considering additional tumors. We think there are some minor modifications we can make, in scheduling and dosages, which might increase the efficacy and reduce toxicity."

Roper said consideration is being given to adding non-Hodgkins lymphoma and breast cancer patients when the studies are resumed.

"I suggest that you work very hard on scheduling and route before you go looking for other tumors," Board member John Mendelsohn said.

Chabner said consideration was being given to NHL because all three treated in the intramural program so far have responded.

"I'm raising the question whether you should even do any other tumors in the intramural studies, considering the toxicities," Mendelsohn said.

Rosenberg responded that the intramural studies are focusing on renal cell, melanoma, colo-rectal and NHL malignancies. "We've only been doing it for one and a half years," Rosenberg said. "It would be a mistake to back off too early. Virtually all of the toxicities are completely reversible. Of course, we're very concerned about the six myocardial infarctions."

In the NCI intramural studies, 104 patients, all with advanced cancer and having failed on other therapy, have been treated with the LAK-IL-2 regimen, Rosenberg told the Board. There have been seven complete responses, 15 partial responses and 10 minor responses (25-50% tumor shrinkage). There was one treatment related death.

Forty five additional patients were treated with interleukin-2 alone, with three treatment related deaths.

Thirty six of the patients on the LAK-IL-2 regimen were renal cell patients, with four complete responses, seven partial and seven minor responses. All received only one cycle of treatment, and Rosenberg said retreatment of the patients has started.

There were 25 melanoma patients, with one complete, five partial and one minor responses. There were 24 colorectal cancer patients, with one complete, five partial and one minor responses. There were two non-Hodgkins lymphoma patients, with one complete and one partial response, plus one more just starting to respond. One each of six other tumor types were treated, with no responses.

A randomized trial was started last April, with patients receiving either aggressive IL-2 alone or LAK-IL-2. Of 21 patients so far receiving IL-2 alone, there has been one complete response and no partial or minor responses. Of the 22 in the LAK-IL-2 arm, there have been two complete, two partial and two minor responses.

Rosenberg said an adjuvant study in stage 2 melanoma has been started. Patients are randomized to one of three arms--surgery only, surgery plus IL-2, and surgery plus LAK-IL-2. So far, of six patients in the surgery only arm, one has recurred. There have been no recurrences among three patients in the IL-2 arm or the five in the LAK-IL-2 arm.

Rosenberg also briefly reported on the status of his new work with tumor infiltrating lymphocytes, which he calls TIL. That is the procedure in which lymphocytes from a patient's tumor are grown in culture with IL-2 then returned. In animal studies, TIL is 100 times as potent as LAK cells, Rosenberg said, suggesting that considerably lower doses may be able to produce equivalent effects, thus reducing toxicity. His report on TIL appeared recently in "Science" (and previously in **The Cancer Letter** and **The Clinical Cancer Letter**).

Rosenberg is designing a clinical study with IL-2, TIL and cytoxan.

Board member Lawrence Einhorn question the use of three arms in the adjuvant melanoma study, especially considering the advent of TIL. "By the time you get the answers, you will probably have the new therapy."

"That is possible," Rosenberg admitted, but suggested that the current studies "will help us learn how better to do the new generation of studies."

Rosenberg defended the results seen to date. Not showing up in the results he reported are "large numbers" of patients with decreases in tumor at one location, with stability elsewhere. They do not qualify for the complete, partial or minor response classifications.

Dan Longo, director of the Biological Response Modifiers Program which is collaborating with Rosenberg's Surgery Branch in the studies, reported on the use of steroids to help control the LAK-IL-2 toxicities.

Longo said patients receiving steroids can tolerate three times the doses of IL-2, apparently without compromising efficacy.

Longo also described an intramural study in which patients receive intraperitoneal LAK-IL-2 treatment, followed after three days by high dose IL-2. That study is being done with ovarian and colon cancer patients.

The six institutions doing the extramural studies are New England Medical Center, Montefiore Medical Center/Albert Einstein

College of Medicine, Loyola Univ. Medical Center, Univ. of Texas Health Science Center (San Antonio)/Audie Murphy VA hospital, Univ. of California (San Francisco),and city of Hope National Medical Center.

NCAB, DeVita Rap Tobacco Industry For Targeting Blacks, Hispanics

Promotional efforts by tobacco companies aimed at Blacks and Hispanics "is a terrible insult" to those populations, NCI Director Vincent DeVita commented at the recent National Cancer Advisory Board meeting after hearing a presentation on cancer prevention awareness programs for minorities.

NCAB Chairman David Korn noted that cigarette promotions were blatantly conducted at a recent meeting of the Congressional Black Caucus.

Lee Monroe, a prevention awareness volunteer who had been heading up a program in North Carolina, said that many exhibits at Urban League meetings are targeted "to things detrimental to Blacks. It raised the question whether the Urban League believed in health promotion."

"How can we win in the Black community against this kind of advertising," DeVita asked Monroe. "Doesn't the Black community consider this an insult?" DeVita said the tobacco industry has a billion dollar a year budget for advertising and promotion directed to Blacks.

"There are groups that may pick this up as an issue," Monroe said.

Board member Louis Sullivan said that Philip Morris paid $50,000 to the Black Congressional Caucus, and that tobacco industry representatives invariably maintain hospitality suites at meetings of Black organizations.

Board member Helen Brown noted that the "tobacco industry is out in force, giving out free samples of cigarettes to Blacks and Hispanics." She suggested that the national "Just say no" campaign against drugs should also include cigarettes.

"It's all offensive to me," Korn said. "It's like pushing sugar on diabetics, or salt on persons with high blood pressure." Korn suggested the reason for targeting of cigarette advertising on Blacks and Hispanics is that those groups are now consuming more cigarettes per capita than whites and do not have the smoking cessation rates of whites.

Rosemary Romano, of NCI's Office of Cancer Communications who heads the Cancer Prevention Awareness Program for Black Americans, described the program and played some TV spots made by singer Aretha Franklin and former pro football star Roosevelt Grier.

Board member Richard Bloch commented that cancer prevention messages have not been getting through in his community (Kansas City), "primarily because they are largely delivered by whites."

Monroe said that when the program was started in North Carolina, "we tried at the start to identify gatekeepers to the Black community to deliver the messages." They looked at several Black organizations and chose the Black Shriners and the Daughters of Israel.

Jane Hoey described the Detroit Model Program in NCI's Cancer Prevention Awareness Program targeted to Black Americans. Involved in that effort are the NAACP, Urban League, a Black businessman's association, city Dept. of Public Health, the public schools, churches, hospitals and libraries.

Meanwhile, the American Cancer Society reported that a study it commissioned found that cancer incidence and mortality is higher among poor Americans, regardless of their race.

Harold Freeman, Harlem Hospital Center and chairman of the ACS Subcommittee on Cancer in the Economically Disadvantaged, presented the report earlier this month on a survey by Donna Funch, SUNY (Buffalo).

The report revealed that the nearly 34 million Americans below the poverty level--23 million whites, 9.5 million Blacks, and 1.2 million of other races--have a relative cancer survival rate 10-15 percent below the American overall rate of about 50%. Controlling for socioeconomic status greatly reduced and sometimes nearly wiped out differences in cancer incidence and survival rates among ethnic groups, the report said.

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.