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PROPAC TO RECOMMEND RECLASSIFICATION OF FIVE LEUKEMIA/LYMPHOMA DIAGNOSIS RELATED GROUPS

The Prospective Payment Commission is recommending that five existing DRGs (Diagnosis Related Groups) for leukemias and lymphomas be reclassified by HHS. The recommendations are part of PROPAC's annual report to

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In Brief

AACR TO HAVE FOUR SYMPOSIA, INCLUDING ONE WITH ASCO; McCONNELL NAMED TRTP DIRECTOR

FOUR SYMPOSIA are planned for the 77th annual meeting of the American Assn. for Cancer Research in Los Angeles: "New Directions in the Use of Biologicals for Diagnosis & Therapy," May 7 (jointly with the American Society of Clinical Oncology), chaired by Ronald Herberman, with presentations by Thomas Waldmann, Steven Rosenberg, Berish Rubin, Robert Bast and David Goldenberg; "Recent Impact of Molecular Genetics on Diagnosis & Prognosis of Human Tumors," May 8, chaired by John Minna, with presentations by Webster Cavenee, Victor Ling and Jeffrey Sklar; "Transmembrane Signaling & Growth Control," May 9, chaired by Bernard Weinstein, with presentations by Tony Hunter, Murray Smigel and Enrique Rozengurt; and "Modulation of Gene Expression During Differentiation," May 10, chaired by Paul Marks, with presentations by Stuart Yuspa, Eric Stanbridge and Douglas Hanahan.... **ERNEST MCCONNELL**, who has been acting deputy director of the National Toxicology Program and acting director of the Toxicology Research & Testing Program in the National Institute of Environmental Health Sciences for more than two years, has been named permanent director of TRTP. The position of NTP deputy director has been abolished (NIEHS Director David Rall is NTP director). TRTP manages the testing and research efforts generated by NTP, including carcinogenesis studies.... **OFFICIAL NAME** of the new cancer hospital at the Univ. of South Florida is the H.Lee Moffitt Cancer Center & Research Institute. The hospital is a five story, 360,000 s.f. building with 162 beds and a 20 bed clinical research unit. Opening is scheduled for May 19.... **BARBARA BLUMBERG**, director of the patient education program in NCI's Office of Cancer Communications, has moved to Fox Chase Cancer Center where she is Patient Education Manager... **ROBERT WINDOM**, Sarasota internist, is another candidate for the position of assistant secretary for health in the Dept. of Health & Human Services. Donald Macdonald has been acting assistant secretary since Otis Bowen was confirmed as HHS secretary in November. The heads of HHS health agencies, including NIH, FDA and HCFA report to the assistant secretary for health.... **JOSEPH LOVETT**, vice president for marketing and sales of Damon Biotech, has been named executive VP.

PROPOSAL WOULD ESTABLISH A SEPARATE ACTUE LEUKEMIA DRG

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HHS Secretary Otis Bowen. The report will recommend that DRGs 400 through 404 be reclassified.

The new groupings would create separate DRGs for acute leukemia patients and those with lymphoma/leukemia. They would also throw out the age grouping that is included in the current DRGs for the diseases, because an analysis of the DRGs show that age is not an important consideration in care costs, PROPAC health analyst Nancy Merrick told **The Cancer Letter.** One of the major changes proposed in the reclassification is the separation of the acute leukemias from the other DRGs because of acute leukemia patients' greater needs during hospitalization, she said.

The recommendation advises that "prior to recalibration, cases currently assigned to DRGs involving lymphoma, leukemia, and other related diagnoses (DRGs 400-404) should be reclassified into one of five newly defined DRGs. The new classification should provide a unique DRG for acute leukemia cases not involving a major operative procedure, eliminate age as a criterion for DRG assignment, and modify present classification based on operative procedure, complications and comorbidity." It adds that "other ways of further improving these DRGs should continue to be explored."

The report notes that "the current lymphoma/leukemia DRGs (400-404) are very heterogeneous in terms of resource consumption. This is evident not only from public comment but also from high coefficients of variation when studying charges and costs."

PROPAC advises that "alternative ways of grouping these cases have been considered in depth. Principal diagnosis, age, major and other operating room procedures, complications/comorbidity and discharge status have been studied. Based on a number of considerations including the intent and design of PPS and the percent of variance in hospital charges explained," PROPAC will recommend these groups:

DRG 400: lymphoma/leukemia with major operating room procedure.

DRG 401: Acute leukemia without major operating room procedure.

DRG 402: Lymphoma/non acute leukemia with other operating room procedure and complication/comorbidity.

DRG 403: Lymphoma/non acute leukemia with other operating room procedure or complication/comorbidity.

DRG 404: Lymphoma/non acute leukemia without operating room procedure or complication/comorbidity.

The report contends that the newly proposed DRGs "are an improvement over the current DRG classification in explaining heterogeneity. Cases in these DRGs should be monitored to determine if additional adjustments will be necessary in the future. Other methods of further improving these DRGs should continue to be studied."

In addition to continuing to consider the DRGs, PROPAC plans to continue considering ways to improve DRG 410 (chemotherapy), another cancer DRG that has been identified as being severely underweighted.

The report and recommendations will be submitted to HHS on April 1. The department is scheduled to issue a response in June. If HHS decides to accept the recommendations, it will recalibrate the weights for the DRGs by putting the patients back into a large pool, assigning them to the DRGs, and looking at the information in order to calculate the new weights.

"It does mean the weights for DRG 401 [acute leukemia] would go up," Merrick said, "because acute leukemia patients do have higher hospitalization costs than other groups of patients" in the five DRGs.

Merrick said the DRGs "have been a real problem." PROPAC began to study six cancer DRGs last summer, and began an in depth analysis last fall. The commission chose the DRGs because they were among those identified by both staff and outsiders as being particularly heterogeneous.

The Assn. of Community Cancer Centers identified the lymphoma/leukemia and chemotherapy DRGs as having insufficient reimbursement weights in a paper presented to the commission last summer. The association asked PROPAC to review the DRGs at that time. ACCC's paper also raised concerns about the impact of Medicare's prospective payment system on the quality of cancer care and research in the U.S.

In a letter to PROPAC Executive Director Donald Young, ACCC detailed its concerns about the use of DRGs for cancer treatment, asserting that "at least several [DRGs] pertaining to cancer are weighted far too low, with a resulting negative and unintended impact on practice patterns, not only in those particular DRGs, but in cancer treatment generally."

It also warned that the prospective payment system's failure "to recognize the longer stays and greater costs involved in clinical cancer research will not only discourage and eventually eliminate most such research, but will

also exert a profoundly chilling effect on the most successful cancer treatment patterns as currently practiced."

An ACCC survey conducted last summer on actual cost, charge and reimbursement data from 16 community hospitals identified DRG 401, leukemia, and DRG 403, acute leukemia, as the most seriously underpaid cancer DRGs. According to the survey, hospitals experienced an average loss per discharge of $1,418.05 for acute leukemia patients and an average loss per discharge of $1,355.43 for leukemia.

An ACCC survey released in January of more than 13,000 discharges at more than 20 community hospitals confirmed the earlier study's findings. The report comparing 72 key cancer DRGs found that DRGs 410 (chemotherapy) and 403 were among the three cancer DRGs producing the greatest loss (**The Cancer Letter**, Jan. 17).

DRG 410 (chemotherapy) "now appears to have a major problem in its current weighting," it said. The DRG was reimbursed at $825,384 below cost on 1,372 discharges.

DRG 403 (lymphoma or leukemia age 70 or above &/or CC) was reimbursed at $450,942 below cost on 796 discharges. DRG 401 (lymphoma or leukemia with minor operating room procedure age 70 or above &/or CC) was reimbursed at $192,532 below cost on 109 discharges. DRG 400 (lymphoma or leukemia with major O.R. procedure) was reimbursed at $94,910 below cost on 119 discharges.

ACCC also found that "adult myelocytic leukemia patients are clearly underweighted," noting that "surely it is obvious that most institutions, even university cancer centers, cannot sustain adequate treatment of the induction phase of these patients on $3,000 for the entire admission," it said.

PROPAC is responsible for consulting with and making recommendations to HHS regarding the need for adjustments to the DRG system; and collecting and assessing information to evaluate the safety, efficacy and cost effectiveness of new and existing medical and surgical procedures, with special attention to be given to updating existing DRGs, establishing new DRGs and making recommendations on relative weighting factors for such groups to reflect appropriate differences in resource consumption.

The commission's three stage interim process for identifying and analyzing issues that may require adjustments in the DRG classifications and/or weights includes the identification of issues from internal assessment or interested third parties; a screening analysis; and an indepth analysis to provide a detailed review of the issues involving options for commission action in developing recommendations to the HHS Secretary.

LAK/IL-2 THERAPY "MAY BE THE END OF KIDNEY CANCER AS A CAUSE OF DEATH"

If given more money in its FY 1987 budget, NCI would expand LAK-IL-2 studies currently underway, especially in patients with kidney cancer, NCI Director Vincent DeVita told House HHS Appropriations Subcommittee Chairman William Natcher (D-Ky.) at last week's budget hearing. Asked by Natcher if he would expand the LAK-IL-2 studies if NCI had more money, DeVita replied, "We're going to have to expand LAK-IL-2. We will have to move quickly into the kidney adjuvant situation. So if we had more money, of course we would do that." NCI also plans to study the therapy as adjuvant treatment for colon cancer as well.

Providing the committee with an update on the regimen developed by NCI Surgery Chief Steven Rosenberg, DeVita said that 71 patients have been treated as of early March. Of those patients, "not a single patient with kidney cancer has failed," he reported.

Investigators have found an overall response rate of 40% with the regimen, a 50% response rate among melanoma patients, and a 100% response rate among patients with kidney cancer.

"It represents a completely different kind of therapy," he said. "I think we may be seeing the end of kidney cancer as a cause of death."

NCI has contracted with six institutions to conduct trials using the exact regimen developed by Rosenberg. The centers are receiving a total of $2.5 million, and are expected to study from 300 to 400 patients in the next year. Cetus is providing the IL-2 free of charge to the centers. Another four institutions are conducting similar trials on their own.

The Div. of Cancer Treatment is planning an extensive, nationwide program of clinical trials with variations of the Rosenberg regimen. If they are all implemented as presently planned, they could cost as much as $100 million over five years.

DeVita told the subcommittee that NCI must develop a way to simplify the regimen in order to decrease the high costs associated with the treatment. "I think we have stumbled on to a way to make it simpler," he said. In addition, "if we can get rid of the side effects, [it] will decrease the amount of care required" for patients on the regimen, thereby resulting in decreased costs. He predicted that, similar to the development of interferon, LAK-IL-2 therapy will become cheaper as the technology is refined.

In addition to identifying the therapy as a high priority area for the institute in the coming year, DeVita cited the LAK-IL-2 project as an example of

scientific opportunities requiring the budgetary flexibility to redirect monies in the middle of a fiscal year.

Asked by Natcher, "Do you have the flexibility to allocate your resources in areas" of need or promising research, DeVita said, "We have had some difficulties." While acknowledging that "numbers have gotten us into some difficulty," he noted that "the committee has always been very responsive." However, the LAK-IL-2 findings came up in the middle of the year. "It would be ideal to move money quickly without going through too many steps."

Natcher also asked if actions by Congress, the Office of Management & Budget, HHS, PHS, NIH or the National Cancer Advisory Board limited DeVita's "effectiveness as commander in chief in the war against cancer?"

"Yes, in [some] cases," DeVita replied. He specifically cited the way the budget is currently apportioned so that portions require a number of steps be taken to gain OMB approval in order to redirect funds. "That can slow us down," he said.

"I think everyone agrees that you should have the flexibility" needed to direct the institute's research activities, Subcommittee member Joseph Early (D-Mass.) told DeVita, adding that he thought the lack of flexibility was as bad as the budget cuts. "Do you have the flexibility as director that you had before the OMB takeover?" Early asked. "I'm worried about flexibility," DeVita replied. "At any [budget] level, I will accept whatever we have to accept," but flexibility remains a concern.

Natcher asked DeVita his opinion on the Administration's proposal to remove the requirement that NIH fund no fewer than 6,100 new and competing grants in 1986.

"In general, I think the movement toward a broader target is better than fixing on 6,100," he said. "I generally prefer stabilization at a broader level" because the mechanism from which developments will come can't always be predicted. "That's why I like 18,000 rather than 6,000 if I had my druthers—the broader the base you're supporting in terms of basic research, the better."

"Should we place a greater emphasis on prevention, clinical trials, or basic research?" Natcher asked. "We got where we are by basic research and I would not change that for a moment," DeVita said, citing examples of research that has moved from the lab to the clinic in a matter of a year. "The danger is missing opportunities—a matter of balance. If you have an opportunity, you should push it." The NCI director again cited LAK cells as an example of an opportunity that presented itself last year.

While DeVita told the committee that basic research will continue to be NCI's top priority, he emphasized that the investigator initiated research grant is not the only mechanism for basic research. "We use many mechanisms [to support basic research] besides the research project grant," he said. "It's much safer to say our number one priority is supporting" basic research.

Natcher also asked DeVita about the effect of reducing FTE (full time equivalent) ceilings to 2,072 in fiscal 1986 and 1987, a 344 drop from the FY 1984 level of 2,416. "We have had to reorder our position priorities and not restaff some," as well as make labs smaller, DeVita said. Asked about the impact of the reductions on NCI's ability to conduct research, he answered, "It makes it more difficult." He added, however, that he would rather "have to run a smaller organization at high speed than run a large one at slow speed...It makes you make hard choices about what you support."

Committee members also discussed staffing levels at the NIH Clinical Center, with Illinois Republican George O'Brien asking "Would it function better if we provided more nurses?"

DeVita responded that the Clinical Center is "functioning well at the level we're at," but that more staff would enable the institute to do more at the facility.

"I worry we're not paying enough attention to adequate [staffing], O'Brien said. "What can I do for you?" DeVita responded that "in the debate over whether to put more in the Clinical Center...you have just joined up on our side."

NIH Deputy Director Thomas Malone told the committee that "recruitment of nurses is always a perennial problem with the Clinical Center. At the present time, we have staff that's able to carry on the [current] programs of the various institutes."

Discussing the Clinical Center's current occupancy rate of 70% to 75%, Malone had earlier advised O'Brien that the nursing staff might not be able to handle the increased workload if the hospital were to increase its occupancy rate.

Under the Administration's proposed budget for FY 1987, NCI would receive $1.158 billion. The institute's Bypass Budget calls for $1.57 billion, a figure that was decreased to $1.463 billion in NCI's budget submitted to NIH, based on the overall HHS budget.

Asked by Early about the proposed 20% cut in competing centers in FY 1986 and 25% reduction in FY 1987, DeVita responded that the decision was made to spread the cut around the centers in order

to maintain the pool rather than eliminate centers.

DeVita told the committee, however, that "it's been a very exciting year." He cited increased understanding of cancer cells, the "new pathology", and trials planned to begin next year with a protein laminin. Cancer cells spread by adhering to the protein, which is found on the lining of blood vessels, he said. Small fragments of laminin have been prepared that can block the cancer cells' laminin receptor and prevent attachment to laminin on the vessel's basement membrane. The treatment approach will be studied in clinical trials in the next year.

"We brought you out a good bill last year, and we're going to bring you out a good bill this year," Natcher said. Noting the difference in NCI's budget appropriated by Congress compared to the amount after sequestration, he said, "It's very hard for us sitting on this committee" to see increases in foreign aid and defense, but decreases in funding for NIH. Acknowleding the seriousness of the budget deficit, Natcher said, "but when they come in and say, 'We want to cut cancer, heart and stroke research,' I don't agree. I think it's a mistake...We ought to spend our money on health and education."

CAUTION ADVISED FOR POST MENOPAUSAL USE OF HORMONAL REPLACEMENT AGENTS

The current enthusiasm for hormonal replacement therapy during menopause for uses such as protection against osteoporosis and certain cancers should be viewed with caution because the protective effect goes away when therapy is stopped, implicating treatment for the rest of a woman's life, Virginia Ernster told a recent meeting of the American Society of Preventive Oncology in Bethesda. She also advised that benefits from hormonal therapy should be weighed against the overall death rate from all causes for women treated with the drugs. Ernster is an associate professor of epidemiology at the Univ. of California (San Francisco) Dept. of Epidemiology & International Health.

Ernster was one of a panel of speakers addressing the risks and benefits of hormonal replacement therapy during menopause at a public health forum at the ASPO meeting.

In addition to its primary use for alleviating menopausal symptoms, estrogen seems to protect postmenopausal women against osteoporosis, Jennifer Kelsey told the meeting. "The evidence is unequivocable about estrogen's protective effect against osteoporosis" as well as fractures of the hip, forearm and vertebrae. Two small studies have suggested that progestins alone have the same protective effect. Kelsey heads the department of epidemiology at the Columbia Univ. School of Public Health.

Estrogen's effect on coronary heart disease has been addressed in 19 published studies, 13 of which show a protective effect with a relative risk of .3 and .4. The effect seems to be related to current use of estrogen, however, with one study showing a relative risk of .3 for myocardial infarction and coronary artery disease among current users, compared to .7 for myocardial infarction and .8 for coronary artery disease among previous users, and a relative risk of 1. for both diseases in women who had never used estrogen.

While the increased risk of endometrial cancer associated with administration of unopposed estrogen appears to be alleviated by the addition of progestins, a number of questions remain unanswered about the hormones, Ernster told the meeting. The major questions concerning progestin use are:

Do progestins reduce to normal the risk of endometrial cancer associated with menopausal estrogens? Do progestins protect against or not influence breast cancer? Do progestins reduce the potential cardiovascular benefits of estrogen by negating its favorable effects on lipid profiles? and, Do progestins affect osteoporosis?

Ernster cautioned that the use of progestins alone may be ill advised because of cardiovascular effects, and emphasized that there were serious methodological flaws in recent studies suggesting that progestins be given for protection against breast cancer.

She noted that unopposed progestins have an adverse effect on lipid profiles. When 19-nor agents are added to estrogen there is a 8% to 20% decrease in HDL below baseline, which is worse than when no estrogens are given at all, she said. When Provera is added to estrogen the beneficial effect of estrogen on HDL is at baseline, or similar to no estrogens.

Questioned about the exclusion of breast cancer from her analysis, Ernster said most of the relative risks hovered around 1 or slightly increased, so relative risk could be excluded. She characterized as dangerous "the current enthusiasm that implicates treatment for the rest of life, since effect goes away when you stop."

She also cautioned that the hormones' uterine effect "may be offset by the overall death" rate, and advised that "it may be important to consider different recommendations for different subgroups."

The widespread enthusiasm for progestin may be premature at this time, she said.

NCI TO SUSPEND CANCER EDUCATION PROGRAM PENDING MODIFICATIONS

NCI will retain its Cancer Education Program in fiscal 1987 at a level of approximately $1 million. The program will be restructured to support short courses and training for target groups, such as minorities.

NCI plans to place a notice in an upcoming issue of the "NIH Guide to Grants and Contracts" notifying prospective applicants that it is suspending receipt of R-25 applications until further notice. NCI will then make another announcement in the future detailing changes to be made in the program before accepting applications again.

Cancer Education Program applications received for February are being reviewed by NCI. New grant applications received for spring review, however, will be returned. While there is no final decision as of yet about grants, the program will certainly be phased down, with the current fiscal year likely to be the final year of funding for awards, whether they are type 2, 3 or 5 awards.

The reshaping of the program is expected to exclude continued support for general oncology curriculum development, reflecting sentiment among NCI Executive Commmittee members that by now, all medical schools should have a cancer care curriculum for which NCI should not have to remain responsible.

The program's support for short courses and special training for minorities and medical students will most likely continue to be supported under the program, although at reduced levels. In recent years, NCI supported approximately 600 medical students for summer appointments under the program. While NCI will probably not be able to support the same number of students, NCI does not anticipate a drastic reduction in the number of students that can be supported under program funding.

Following the suspension of the program, NCI will take proposals for modifications to the program to the Div. of Cancer Prevention & Contol's Board of Scientific Counselors in May for discussion on what modifications should be made. r ~~discussion on~~

Most of the fiscal 1986 Type 5 awards have start dates of July 1, and will probably be funded at about half of their recommended levels. They will then have a year until fiscal 1987, by which time the program will be restructured. FY 1986 awards already made in January, February, March and those made in April will be funded at the recommended level. The program's present structure will continue through FY 1986, but fiscal 1987 "is a whole new ball game," one NCI official said.

NLM'S "GRATEFUL MED" USER FRIENDLY SOFTWARE SYSTEM AIDS DATA SEARCHES

The National Library of Medicine has developed a software package designed to help physicians and other health professionals gain simple, direct access to its computerized databases previously accessible on NLM's computers only by trained searchers and through other libraries.

Known as "GRATEFUL MED," the software is designed to greatly ease computer searching. The software is used with an IBM PC or compatible computer equipped with a Hayes (or compatible) modem to search and retrieve information from the library's databases.

The user types in a query, such as an author's name or subject words, on a simple format screen, and the program takes over. GRATEFUL MED calls up the library's computers, logs on, enters the queries specified by the user, retrieves references and abstracts, and transfers them to the floppy disk where they may be reviewed at leisure. Because the user is not involved in the brief online session, computer connection time is minimal.

GRATEFUL MED comes on one floppy disk with simple instructuons and an application for a user code. There is no fee to join or monthly minimum charge. Users are billed monthly for their use of the system, approximately $20 per hour for connect time. NLM reports that the cost for most searches averages about $1 to $4.

Users can specifically access NLM's MEDLINE and CATLINE databases, as well as NCI's PDQ (Physician Data Query) with the new software package. More than 6 million references and abstracts for journal articles from 1966 to the present, and 600,000 catalog records for books, may be searched with the software and a personal computer.

The system is intended to enable health care professionals to search the computerized data bases with ease, and a minimal amount of computer time by helping users construct their search, talking to the main computer search program ELHILL on the user's behalf, accepting and storing the ELHILL search results, helping the user evaluate the results and suggesting further search terms from MESH (NLM's controlled vocabulary).

For example, after a search is completed, GRATEFUL MED recommends MESH headings that may provide a more comprehensive search on the basis of the MESH headings attached to the citations. MESH headings are used by professional indexers to describe the article.

Users may work directly with ELHILL through GRATEFUL MED in "pass through" mode.

NLM gave copies of the user friendly interface to approximately 150 science writers who attended the library's sesquicentennial in February.

GRATEFUL MED software is sold by the National Technical Information Service for $29.95 (plus $3 handling) per copy. The order number is PB86-158482. Orders should be sent to the National Technical Information Service, U.S. Dept. of Commerce, 5285 Port Royal Rd., Springfield, Va. 22161. NTIS also handles the billing for usage of the system. Technical queries about the system may be directed to the MEDLARS Management Section, National Library of Medicine, Bethesda, Md. 20894, phone 301-496-6193.

FDA COMMITTEE APPROVES NDA FOR MITAXANTRONE FOR BREAST CANCER

The Food & Drug Administration's Oncologic Drugs Advisory Committee recommended approval of two new drug applications last week—mitoxantrone as alternate therapy for advanced breast cancer, and adding adult acute lymphocytic leukemia to previously approved indications for daunorubicin.

The committee last year had rejected Lederle Laboratories' request for approval of mitoxantrone, which it will market under the trade name Novantrone. Committee members said then that the studies supporting the NDA were not sufficiently mature to support the contention that mitoxantrone was sufficiently close to equal in effectiveness to adriamycin and significantly less toxic to warrant marketing it as an alternative to adriamycin.

This time, Lederle and investigators who participated in the studies comparing mitoxantrone to adriamycin convinced a solid majority of the committee that the compound should be approved for marketing. The vote for approval was 9-2, with Charles Moertel and Thomas Fleming still not convinced.

Moertel based his objections on what he said was failure of the studies to prove mitoxantrone is as effective as adriamycin, "going by the response rates." Also, he argued that the results were distorted because "50 percent of the patients entered were lost to analysis. I hope we won't set a precedent using studies like these."

Moertel said that one of the studies, which showed a significant improvement in the cardiotoxicity curve for mitoxantrone over adriamycin, was flawed because it "assumed the appropriate dose ratio was five adriamycin to one mitoxantrone. I question how realistic the five to one ratio is. If it were four to one, the cardiotoxicity curves would be right on top of each other."

Moertel also noted that reductions from recommended doses also could have affected the results. However, Robert Benjamin, one of the investigators involved in the studies, said, "Make it three to one, as conservative as you want, mitoxantrone still has less cardiotoxicity than adriamycin."

Fleming contended that response rates from the four studies sponsored by Lederle were as much as 50 percent higher for adriamycin, although acknowledging that the difference was not statistically significant. "They are close to statistical significance," he said. "The bottom line is survival. One study is borderline for 50 percent better survival with adriamycin. One study is borderline for equality. A large number of patients were ineligible or inevaluable, and a fair number lost to followup. There is significant evidence against equality."

Committee member Susan Pitman suggested that "the problem is not so much cardiotoxicity but alopecia." The four studies found that there was very little hair loss with mitoxantrone, while that has always been a major problem with adriamycin. Fear of losing their hair frequently causes women to delay starting chemotherapy, and sometimes even to avoid it entirely, she said. "I think we could possibly see an improvement in the therapeutic index, with women accepting treatment up front because of no hair loss."

"We spend more time talking about toxicity than we do to explain the value of therapy," committee member George Canellos said. "Palliative treatment is important. But palliation should not be worse than the disease."

Committee member Rodger Winn observed that approval of mitoxantrone would permit "customizing of treatment. It offers options for older women."

Committee member Robert Bast said he worried about "survival as an endpoint. Adriamycin probably does not add much."

"Survival is not a proper endpoint," committee member Paul Carbone said. "Many times, we need to make women more comfortable. Toxicity is important. Despite my reservations, I think this might be a useful drug."

The studies also found that mitoxantrone produced far less nausea and vomiting along with less myelosuppression and cardiotoxicity.

Wyeth Laboratories, which markets daunorubicin under the trade name Cerubidine, presented evidence from one study which showed that the drug produces an improvement in complete remission rates in adult ALL. The committee went along with adding that disease to the previously approved indications for the drug.

RFAs AVAILABLE

RFA CA-86-09
Title: Inheritance and markers of colorectal cancer and polyps
Application receipt date: June 15

The Organ Systems Program of the Div. of Cancer Prevention & Control invites grant applications for studies aimed at identifying and comparing populations at high risk for colorectal cancer. A major goal of this announcement is to solicit applications which integrate research on the genetic epidemiology of adenomatous polyps with new findings on markers for colorectal cancer.

A small percentage of colorectal cancer cases is associated with inherited syndromes that display well known patterns of genetic segregation and inheritance. A much larger percentage of cases exhibits familial aggregation but displays no readily apparent pattern of mendelian inheritance. This latter group represents a significant fraction of colorectal cancer cases. Further delineation of this group by polyp and marker studies would lead to direct clinical benefits. There is a need for collaborative investigations which would further identify polyp etiologic factors and clinically useful markers for high risk populations. The adenomatous polyp is a much more common lesion than colorectal cancer, and polyps are thought to occur in response to the same genetic and environmental factors which lead to malignancy. Thus, polyps from a spectrum of populations at high risk for colorectal cancer would provide valuable clinical material for testing cancer markers and for testing hypotheses of gene-environment interactions.

Human colon cancer is a good system in which to determine in a rigorous way whether new reagents, such as monoclonal antibodies or cloned gene sequences, can be of significant value in the diagnosis, prognosis and classification of solid tumors. The identification of high risk groups in addition to the readily recognized genetic syndromes would permit close monitoring of a much larger segment of the population at risk for colorectal cancer. The subsequent application of preventive measurers, early removal of preneoplastic lesions and early surgical intervention would reduce incidence and improve prognosis in these groups.

The overall goal of this initiative is to stimulate the development of collaborative studies between marker experts and clinical research groups having access to populations at high risk for colorectal cancer. A specific objective is to define population groups which differ in their inherited risk for colorectal cancer. Emphasis is placed on familial aggregates of adenomatous polyps and colorectal cancer in order to extend observations from the currently well known high risk genetic groups into the larger population of sporadic colon cancer. Biochemical, immunologic, genetic, cytogenetic and molecular markers will be identified and applied to individuals in these defined population groups to identify which individuals are predisposed to adenomatous polyps and colorectal cancer, and to classify stages in the progression from normal colonic mucosa to invasive and metastatic carcinoma.

A long range goal would be to define a major gene for adenomatous polyps, or to define a marker that might lead to the successful chromosomal mapping of a colorectal cancer gene.

NCI plans to fund up to five awards for project periods of three years and has set aside $1 million for the initial year of funding. The expected starting date for these awards is Dec. 1, 1986. Renewability would be dependent on successful competition in the regular NIH grant review system. Although this program is provided for in the financial plans of NCI, awards are contingent upon availability of funds for this purpose and the receipt of applications of high scientific merit. There are no plans for future reissuance of this RFA.

A more detailed RFA is available upon request from, and inquiries may be directed to, Dr. Vincent Cairoli, Organ Systems Section, Cancer Centers Branch, NCI, DCPC, Blair Bldg Rm 727, Bethesda, MD. 20892, phone 301-427-8818.

Applicants are encouraged to submit letters of intent, identifying the poposed principal investigator and collaborating institutions, to Cairoli by April 15. A letter of intent is not binding and will not be used in the review of any application submitted.

The concept from which this RFA was derived was approved by the Div. of Cancer Etiology Board of Scientific Counselors last fall and reported in The Cancer Letter Nov. 1, pages 1-3.

RFP NIH-ES-86-02
Title: Support for chemical nomination and selection process of the National Toxicology Program
Deadline: (Listed in the RFP)

The National Institute of Environmental Health Sciences is soliciting proposals to support the NTP chemical nomination and selection process through the preparation of NTP executive summaries on chemicals nominated to NTP for toxicological testing. The development of summary information and data on chemicals previously tested by NTP for one or more toxic endpoints and on structural analogs of such chemicals to aid NTP staff in determining which of these chemicals may be candidates for further NTP testing, and the collection, sumarization entry of relevant information and data on nominated chemicals into the NTP CHEMTRACK data base. Contact Thomas Hardee, contract specialist, NIEHS, PO Box 12874, Research Triangle Park, N.C. 27709.

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams
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