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PO Box 9905 Washington DC 20016 Telephone 202-362-1809

ODAC Supports Approval For Taxotere In Breast Cancer, Hycamtin In Lung Cancer

The FDA Oncologic Drugs Advisory Committee earlier this week recommended full approval to Taxotere (docetaxel) and expanded the drug's indication to cover "the treatment of patients with locally advanced or metastatic breast cancer who have failed previous chemotherapy."

The advisory committee voted unanimously, 8-0, to change the drug's status from "accelerated approval," which is conditional on conduct

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In Brief:

Women's Health Group Asks Magazines To Stop Accepting Tobacco Advertising

STOP ACCEPTING tobacco advertising, the Society for the Advancement of Women's Health Research has asked publishers of all women's magazines. The society listed 17 magazines, most of which profess concern for women's health, which contain cigarette advertising. "How can publications that accept tobacco advertising say they are committed to improving the well being of women?" asked **Phyllis Greenberger**, executive director of the society. She noted that research shows that the rate of lung cancer is 20 to 70 percent higher in women than men; that the carcinogenic effects of smoking impact women more severely than men; and that 73 percent of women prefer women's magazines as a source of health information. . . . **CLARA BLOOMFIELD**, director of the Ohio State Univ. Comprehensive Cancer Center and codirector of the Arthur G. James Cancer Hospital & Research Institute, has been selected by the Medical & Biological Sciences Alumni Association at the Univ. of Chicago to receive its 1998 distinguished service award. . . . **FOX CHASE** Cancer Center has broken ground for its 120,000 square foot, $38 million Prevention Pavillion, which will house the center's Research Institute for Cancer Prevention. **Robert Young**, Fox Chase president, said "the future of cancer research rests with learning how to prevent cancer before it ever strikes." Fox Chase programs that will be located in the new facility will include state of the art genetic testing, screening, and counseling. . . . **SELMA SCHIMMEL**, who created Vital Options, an organization for young adults with cancer, is seeking nominations for "Vital Lives: A list of Cancer Survivors." "This is an opportunity for loved ones to recognize cancer survivors and for the survivors to celebrate their own triumphs," Schimmel said. The list is open to anyone who has been diagnosed and treated for cancer and

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ODAC Okays ONTAK Approval, Votes Down Bladder Treatment

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of further studies, to full approval.

In addition to recommending removal of the contingency, ODAC voted 7-1 to broaden the Taxotere indications, which in the past said the drug was appropriate for patients "who have progressed during anthracycline-based therapy or have relapsed during anthracycline-based adjuvant therapy."

The new indication would eliminate references to anthracycline-based therapy after the company presented results of a side-by-side trial of Taxotere vs. doxorubicin. The trial demonstrated that Taxotere increased the median time to disease progression.

In its application to FDA, the drug sponsor, Rhone-Poulenc Rorer Pharmaceuticals Inc., of Collegeville, PA, made a commitment to complete two phase III trials: a trial comparing three doses of Taxotere and a side-by-side trial of Taxotere and the Bristol-Myers Squibb drug Taxol.

Other Recommendations

In other recommendations during the ODAC June 1-2 session:

—The committee recommended approval of Hycamtin (topotecan hydrochloride for injection) for the second-line treatment of sensitive small cell lung cancer. Hycamtin is approved in the treatment of ovarian cancer after failure of initial or subsequent chemotherapy. The drug is sponsored by SmithKline Beecham, of Philadelphia.

—The committee recommended approval of ONTAK (DAB389IL-2, IL-2 Fusion Protein or Denileukin diftitox) for treatment of adult patients with recurrent or persistent cutaneous T-cell lymphoma. The drug is sponsored by Seragen Inc., of Hopkinton, MA, but is being transferred to Ligand Pharmaceuticals Inc., of San Diego.

—The committee voted against approval of AD 32 (valrubicin 40 mg/mL) for the treatment of refractory carcinoma in situ of the urinary bladder. The drug is sponsored by Anthra Pharmaceuticals. The committee voted 10-0 with one abstention that the studies presented by the company did not present sufficient data to support approval, considering the potential risk of invasive or metastatic disease when cystectomy is delayed.

The Taxotere Trials

Taxotere received a conditional approval in May 1996 that required the company to complete two phase III trials in metastatic breast cancer.

Once conducted, these studies established Taxotere as the first anticancer agent to show superior response rate and predictable safety profile relative to doxorubicin, and the first single agent to demonstrate increased survival among patients with advanced breast cancer when compared to the combination of mitomycin C plus vinblastine, the company said.

The first of these randomized phase III multicenter trials compared Taxotere as a single agent to mitomycin C in combination with vinblastine in patients with metastatic breast cancer that has failed an anthracycline containing regimen.

The one-year survival rate among breast cancer patients treated with Taxotere was 49 percent, compared to 33 percent for those treated with the combination mitomycin C and vinblastine.

One year after therapy, 50 percent more patients treated with Taxotere were alive compared to those treated with the combination therapy. The 18-month survival rate was 33 percent for Taxotere patients, compared to 21 percent for mitomycin C plus vinblastine patients. Survival at 18 months was nearly 60 percent higher among the Taxotere treated patients.

"The increase in overall survival for this study is impressive," said Jean Marc Nabholtz, chairman,

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World Wide Web: http://www.cancerletter.com

Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg

Editorial: 202-362-1809 Fax: 202-362-1681
PO Box 9905, Washington DC 20016
E-mail: kirsten@cancerletter.com or paul@cancerletter.com

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724

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Founded Dec. 21, 1973 by Jerry D. Boyd

Northern Alberta Breast Cancer Program and senior medical oncologist, Cross Cancer Institute, Edmonton, Alberta, Canada, and lead investigator of the study. "Taxotere as a single agent clearly demonstrated superiority to the combination therapy. This is very good news for patients with metastatic breast cancer whose cancer has progressed during or after anthracycline treatment."

The second randomized phase III study presented was a multicenter trial comparing Taxotere to doxorubicin in patients with metastatic breast cancer whose disease failed a regimen containing an alkylating agent. Patients treated with Taxotere showed a 50 percent better overall response rate compared to patients treated with doxorubicin (48 percent for Taxotere vs. 33 percent for doxorubicin).

Among resistant patients (those with disease that had progressed on previous regimens containing alkylating agents) and those with liver metastases, the response rates were significantly higher than doxorubicin (47 percent vs. 24 percent for resistant patients, and 54 percent vs. 27 percent for patients with liver metastases).

"The results of this study would seem to indicate that Taxotere is more active than doxorubicin in patients with advanced breast cancer," said John Crown, of St. Vincent's Hospital in Dublin, Ireland, and one of the study's lead investigators.

"Patients treated with Taxotere experienced an efficacy advantage and equivalent quality of life compared to those treated with doxorubicin," Crown said.

In patients with normal liver function, side effects reported to date include neutropenia, thrombocytopenia, anemia, fluid retention, hypersensitivity, nausea and diarrhea.

A premedication regimen with corticosteroids is recommended in order to prevent or reduce hypersensitivity and fluid retention. Taxotere is not appropriate therapy for patients with significant liver impairment.

Hycamtin for Small Cell Lung Cancer

ODAC recommended approval of Hycamtin, a topoisomerase I inihibitor, for the second-line treatment of sensitive small cell lung cancer after reviewing data from four trials in patients with relapsed small cell lung cancer.

Hycamtin is approved for use in the treatment of ovarian cancer after failure of initial or subsequent chemotherapy.

In a randomized, phase III, comparative trial, Hycamtin as a single agent showed comparable efficacy to cyclophosphamide, doxorubicin, and vincristine (CAV), a drug combination for the treatment of relapsed small cell lung cancer. Median survival and time to progression were also comparable for both treatment groups.

Also, the sponsor presented three studies that evaluated Hycamtin as a single agent in sensitive and refractory SCLC.

"Since most small cell lung cancer patients will eventually relapse and become difficult to treat, there is a need for new agents such as Hycamtin that can be used to treat patients, particularly those who have failed first-line therapy," said Joan Schiller, associate professor, University of Wisconsin Comprehensive Cancer Center, and the lead U.S. study investigator for the phase III clinical trial. "There is currently no standard treatment for this malignancy, which is one of the most deadly cancers among both men and women.

"Results from several clinical trials involving patients treated with Hycamtin have been very encouraging," Schiller said.

The panel based its decision in part on a large phase III, randomized clinical trial that was conducted at 44 centers in North America, Europe, and South Africa and involved 211 patients who had relapsed at least 60 days after their initial treatment.

Patients received either an intravenous infusion of Hycamtin 1.5 mg/m^2 as a single agent therapy for five consecutive days every three weeks or CAV (a combination therapy consisting of cyclophosphamide 1,000 mg/m^2, doxorubicin 45 mg/m^2, and vincristine 2 mg) administered intravenously on day one every three weeks.

A greater percentage of Hycamtin-treated patients responded to treatment (24.3 percent vs. 18.3 percent), although this difference was not statistically significant. Tumors were assessed by radiologic evaluation and required independent confirmation.

Median survival and time to progression were comparable for both treatment groups.

Furthermore, more patients treated with Hycamtin reported improvement in disease-related symptoms than patients treated with CAV.

A significantly higher percentage of patients who were treated with Hycamtin versus CAV reported an improvement in the following symptoms: shortness of breath (p=0.002), fatigue (p=0.032), hoarseness (p=0.043), and anorexia (p=0.042).

Improvement was defined as improvement over baseline sustained for at least two consecutive courses. In addition, significantly fewer Hycamtin-treated patients (p=0.023) experienced interference with daily activities.

Of the other four symptoms measured, improvements were numerically superior for Hycamtin-treated patients (chest pain, cough, insomnia; p=not significant), while improvement in hemoptysis was numerically superior for patients treated with CAV (p=not significant), although this symptom was not very frequent in either group.

Data were also reviewed from three open label, non-comparative trials involving 319 patients with recurrent or progressive small cell lung cancer after treatment with first-line chemotherapy. These three studies supported the results of the phase III study.

The main side effect experienced by Hycamtin in clinical trials was neutropenia (suppression of white blood cells), which was predictable, non-cumulative, and manageable. Non-hematologic side effects were generally mild; the most commonly observed events were low-grade nausea, vomiting and diarrhea.

Hycamtin is contraindicated in patients who have a history of hypersensitivity reactions to Hycamtin or any of its ingredients and should not be used in patients who are pregnant or breast-feeding, or those with severe bone marrow depression.

The drug is under clinical investigation for non-small cell lung, breast, colorectal and pediatric cancer, lymphoma, myeloma and leukemia, as well as first-line combination chemotherapy in ovarian cancer, the company said.

ONTAK for CTCL

ODAC was expanded for consideration of ONTAK (DAB389IL-2, IL-2 Fusion Protein or Denileukin diftitox) for treatment of adult patients with recurrent or persistent CTCL. The committee included consultants representing biologics and dermatology, as well as an CTCL expert from NCI.

According to an FDA review of company data, ONTAK produced an overall response rate of 30 percent and a complete response rate of 10 percent in 71 patients with previously treated CTCL in stages Ib through IV.

The median response was 4.4 months. In a phase I dose-escalating study that enrolled 35 patients, the overall response rate was 37 percent and complete response rate was 14 percent.

Thirty-nine percent of patients experienced grade 3 adverse events, and another 30 percent experienced grade 4 adverse events, which included constitutional symptoms, hypersensitivity reactions, vascular leak syndrome, dehydration caused by nausea and diarrhea.

The committee first voted 14 to 0 that the clinical results cited in the Biologic License Application for ONTAK are "reasonably likely to predict clinical benefit in patients with CTCL who have failed one or more systemic therapies."

Turning to the second of three questions, the committee once again voted unanimously that the toxicity associated with ONTAK treatment is "acceptable, given the response rates and durations of responses observed."

By a vote of 12 to 2, the panel also recommended that treating physicians should decide the appropriate dose within a prescribed dose range.

If approved, ONTAK will be the first therapeutic specifically approved by the FDA for CTCL.

"Overall, the outlook for patients with advanced CTCL is poor, especially those late-stage patients with organ or lymph node involvement, whose median survival is less than three years," said Paul Bunn, director of the University of Colorado Cancer Center in Denver and CTCL specialist.

"Any agent that can reduce tumor burden and/or improve symptoms in these patients, as ONTAK does, is sorely needed," Bunn said.

The rights to ONTAK are in the process of being transferred from Seragen Inc. (OTC Bulletin Board: SRGN) to Ligand Pharmaceuticals Inc. (Nasdaq: LGND). On May 11, Ligand and Seragen said they signed a definitive agreement under which a wholly owned subsidiary of Ligand would merge with Seragen.

Ligand announced at the same time that it had signed a definitive asset purchase agreement to acquire the assets of Marathon Biopharmaceuticals, LLC, which provides product development, clinical trials and manufacturing services to Seragen under a service agreement.

The net effect of these agreements, if the transactions are completed, is to provide Ligand with worldwide rights to ONTAK, as well as five additional fusion proteins—DAB389EGF, DAB389IL-4, DAB389IL-6, DAB389CD-4, and DAB389MSH—which may have implications in other disease states.

In Congress:

Funds Unavailable To Provide Big Increase To NIH This Year

As markup of appropriations bills begins, Congress has little room for generosity.

The allocations for Labor, HHS and Education subcommittees in the House and the Senate have been capped as a result of last year's balanced budget agreement, and there is no mechanism in sight for additional funds to be channeled to biomedical research, Capitol Hill observers say.

In the House, the markup for the Labor, HHS & Education bill is tentatively scheduled to begin the last week of June. The Senate markup has not been scheduled.

The House allocation is $81.896 billion, $279 million below the Senate allocation of $82.175 billion. Considering that the allocations are low and inflexible, many Capitol Hill observers are unclear about how the Administration would be able to meet its goal of increasing the NIH budget by $1.15 billion next year and doubling the Institutes' budget in five years.

Senior Administration officials pledged that if tobacco funds do no materialize, the increases for NIH would be funded from tax revenue (**The Cancer Letter**, Feb. 6).

Dave Kohn, a spokesman for Rep. John Porter, chairman of the House Labor, HHS and Education Appropriations Subcommittee, said the subcommittee is not counting on any windfalls.

"Mr. Porter is proceeding with the business of his subcommittee, and is not counting on tobacco revenues being a part of these deliberations," Kohn said to **The Cancer Letter**.

"Mr. Porter would like to see a significant increase for NIH, but clearly this is going to be a difficult year for all appropriations bills, including this one," Kohn said.

At a recent subcommittee hearing, Porter told the testifying Nobel laureates that discretionary spending in fiscal 1999 is likely to be so tight that the incremental increases needed to double the NIH budget in five years would have to begin next year.

Though a 15 percent increase for NIH does not seem likely at this point, belt-tightening is unlikely also, Capitol Hill sources say.

"I know that Mr. Porter would not stand for a retrenchment that would impede the work going on at NCI and NIH," Kohn said.

Food & Drug Administration:

Consolidation Plan Intended To Save Money, Official Says

A senior FDA official said the agency's plan to combine the Office of Special Health Issues with the Office of Consumer Affairs is intended to bring about savings in the running of the two offices while preserving the same level of service.

"We determined that we could achieve efficiencies by bringing together our consumer-focused components, while preserving the special focus of each of those organizations," Sharon Smith Holston, FDA Deputy Commissioner for External Affairs, wrote in her official response to a letter from Rep. Joe Barton (R-TX), chairman of the Subcommittee on Oversight and Investigations of the House Committee on Commerce. (**The Cancer Letter,** May 22).

In recent weeks, cancer and AIDS groups were critical of the agency's plan to merge the special health office, which was created specifically to meet the needs of critically ill patients, with the consumer affairs office, which responds to a broad range of food, drug, and cosmetics issues.

In a letter to Barton, Holston wrote that the changes age needed because the operating budget of the agency's Office of External Affairs has been reduced by 25 percent, and the number of full time equivalent positions decreased by 10 percent.

"We determined that we could achieve efficiencies by bringing together our consumer focused components, while preserving the special focus of each of those organizations," Holston wrote. "Through leveraging the resources of both components, we believe it may even be possible to provide a greater level of support and service to this important segment of our constituency."

A copy of the letter, dated May 28, was obtained by **The Cancer Letter**.

Holston wrote that at this point the "re-design" of the office involves agency employees who interact with consumers and at a later date the agency plans to involve the advocacy groups.

"It has been brought to our attention that many external groups are keenly aware of our plans, and are interested in sharing their perspectives and ideas on this effort," Holston wrote. "We will be scheduling one or more formal meetings where groups and individuals will have an opportunity to provide their input to our process."

On June 9, Holston will have an opportunity to discuss this issue with an ad hoc coalition of advocacy groups that will meet in Washington to discuss the proposed merger. The meeting, to which Holston has been invited, was organized by Carl Dixon, president and executive director of the National Kidney Cancer Association, and Peggy McCarthy, executive director of the Alliance for Lung Cancer Advocacy, Support and Education.

Funding Opportunities:

RFAs Available

RFA CA-98-006

Title: **Advanced Technology Radiation Therapy Clinical Trials Support**

Letter of Intent Receipt Date: July 7

Application Receipt Date: Aug. 11

This Request for Applications is to solicit applications to generate a resource that will facilitate the conduct of NCI sponsored clinical trials in 3-dimensional radiation therapy treatment planning and delivery (3D-CRT), stereotactically directed radiation therapy, intensity modulated radiation therapy (IMRT), and brachytherapy in both pediatric and adult patients.

The Radiation Research Program, NCI Div. of Cancer Treatment and Diagnosis, invites applications for projects to generate a resource for support of high technology radiation therapy clinical trials. Such support should include credentialing of institutions to participate in these trials, developing basic technical and quality assurance criteria for each protocol assessed, providing prospective review of treatment plans to assure that they are within protocol specifications. Such support should also include development and maintenance of a comprehensive database of diagnostic images, dose-volume histograms, tumor and normal structure definitions to be correlated with treatment outcomes.

Total project period may not exceed 3 years. Anticipated award date is April 1999.

The use of image based radiation teletherapy treatment planning has grown substantially over the past few years. The rapid growth in computer processing power and concomitant decrease in cost has made this possible. This allows the radiation oncologist to visualize the radiation treatment plan directly on the patients diagnostic CT or MRI with the tumor and critical normal structure in place. Fashioning a three dimensional view of any single structure is also possible. Diagnostic imaging can also be used to guide placement of brachytherapy sources. Once the digital images and treatment parameters are available they may be centrally archived for a quantitative analysis of doseolume relationships for long term outcomes of both tumor control and normal tissue toxicity.

Planning and delivering radiation with these advanced technologies is not as straight forward as with conventional techniques. More precise definition of tumor and normal tissue is necessary as is the need to evaluate all aspects of the treatment plan in three dimensions instead of the more familiar two dimensions. Multi-institutional clinical trials require a consistent quality assurance program for 3D CRT and brachytherapy treatment plans.

The purpose of the development of a central quality assurance resource is to eliminate the need for individual clinical trials groups to assemble a resource intensive quality assurance center which each individual group may not be able to use optimally. A centralized resource will ensure that appropriate personnel and equipment are available when needed and that appropriate procedures and criteria are developed. With the availability of full digital data for tumor and normal tissue volumes, it will be necessary to establish a database for that information that may be made available with the NCI providing any needed input regarding allocation of available resources.

Inquiries: Richard Cumberlin, Div. of Cancer Treatment and Diagnosis, NCI, 6130 Executive Blvd Suite 800-MSC 7440, Bethesda, MD 20892-7440. Tel: 301/496-6111, fax: 301/ 480-5785.

Program Announcements

PAR-98-068

Title: **Engineered Isogenic Cell Lines With Relevant Cancer Targets**

Letter of Intent Receipt Dates: July 2, 1998, and March 5, 1999

Application Receipt Dates: Aug. 7, 1998, and April 9, 1999

This PA encourages the small business community to develop isogenic cell lines in which functions of a molecular activity or pathway found in human tumors can be analyzed in pair wise fashion. Such cell lines could be used for drug screening with the intent of identification of compounds which influence the action of the identified target. The end result of the PA supported projects would be a series of genetically engineered screening models which the small businesses could market directly or utilize in a license agreement or other type of collaboration. Any small business, independently owned by US citizens and located in the US, may apply.

Support for the PA is through the SBIR and STTR mechanisms which are set aside programs. Applications can be submitted for support as Phase I STTR (R41) or Phase I SBIR (R43) grants: Phase II STTR (R42) or Phase II SBIR (R44) grants; or under the SBIR/STTR FAST-TRACK option. Phase II applications in response to this PA will only be accepted as competing continuations of previously funded NIH Phase I SBIR/STTR awards. The Phase II proposal must be a logical extension of the Phase I research.

Information on the FAST-TRACK process and the

Omnibus Solicitations are available at: http://www.nih.gov/grants/funding/sbir.htm

The normal level of support and period of time for a Phase I SBIR award is $100,000 and six months; for Phase II SBIR award, $750,000 and two years. The normal level of support and period of time for a Phase I STTR awards is $100,000 and one year; for a Phase II STTR award is $500,000 and two years. However, applicants may propose longer periods of time and greater amounts of funds if necessary for completion of the project.

Inquiries: George Johnson, NCI Div. of Cancer Treatment and Diagnosis, 6130 Executive Blvd Rm 841, Bethesda, MD 20892-7456. Tel: 301/496-8783, fax: 301/402-5200, email: gj16m@nih.gov

PAR-98-067

Title: **Innovative Technologies For The Molecular *Analysis Of Cancer: Phased Innovation* Award**

Letter of Intent Receipt Dates: July 2, Nov. 5, 1998, and March 5, 1999

Application Receipt Dates: Aug. 7, Dec. 10, 1998 and April 9, 1999

NCI invites applications for research projects to develop novel technologies that will support the molecular analysis of cancers and their host environment in support of basic, clinical, and epidemiological research. Technology encompasses methods and tools that enable research including, but not limited to, instrumentation, techniques, devices, and analysis tools (e.g., computer software). Technology is distinct from resources such as databases and tissue repositories. Applications for support of such resources will not be considered to be responsive to this program announcement.

Technologies solicited include those that are suitable for the detection of alterations and instabilities of genomic DNA; monitoring of the expression of genes and gene products; analysis and detection of the cellular localization, post translational modification, and function of proteins; and monitoring of major signal transduction networks involved in cancer. This PA is intended to support the development of all required components of fully integrated systems for analysis including front end preparation of sample materials from cells, bodily fluids, and tumor specimens; novel chemistries or contrast agents; molecular detection systems; data acquisition methods; and data analysis tools. Technologies under consideration include those that will support molecular analysis either in vitro, in situ, or in vivo (by imaging or other methods) in the discovery process, as well as in clinical application.

This program will utilize the phased innovation award mechanisms (R21 and/or R33) to allow expedited review of applications and expedited transition of successful technology research to an expanded development phase. Small businesses are encouraged to consider a parallel program announcement (PAR-98-066) of identical scientific scope that utilizes the SBIR and STTR mechanisms with accelerated review and transition, as well as cost and duration requirements comparable to the phased innovation awards.

Support for this program will be through the NIH exploratory/developmental research grant (R21) and the exploratory/developmental research grant Phase 2 (R33). The R33 is a newly established NIH grant mechanism to provide a second phase for the support of innovative exploratory and development research initiated under the R21 mechanism. Conversion of the R21 to the R33 phase will be expedited and based on completion of negotiated milestones.

For combined R21/R33 applications, the R21 phase may not exceed $100,000 direct costs per year. R21 budgets can exceed this cap to accommodate indirect costs to subcontracts to the project. Although the R33 application has no official budgetary limit, applications requesting in excess of $500,000 dollars direct costs in any single year of the grant period require prior approval before submission. It is strongly recommended that applicants contact NCI staff at an early stage of application development to convey critical information, such as potentially large budget requests or to discuss programmatic responsiveness of the proposed project. Early contact with NCI staff is particularly critical relative to this PA since it utilizes a new grant mechanism (R33) as well as an expedited review procedure.

Inquiries: Carol Dahl, Office of Technology and Industrial Relations, NCI, Building 31, Room 11A03, 31 Center Drive MSC 2590, Bethesda, MD 20892-2590. Tel: 301/496-1550, fax: 301/496-7807, email: carol_dahl@nih.gov

PA-98-069

Title: **Cancer Pharmacology *and* Treatment in Older Patients**

The National Institute on Aging and the National Cancer Institute invite research grant applications to expand the understanding of the pharmacology of antineoplastic agents in older patients. This research initiative specifically addresses the disposition, efficacy, and effectiveness of anti-cancer agents in older cancer patients. The goal of this PA is to stimulate research to improve treatment and care of older persons affected with cancer with explicit attention to aging and old age and their effects on anti-cancer therapy pharmacokinetics and pharmacodynamics. Support is through the NIH R01 mechanism and the exploratory/developmental grant (R21) mechanism. R21 awards are limited to $100,000 direct costs per year (up to two years).

The PA emphasizes research to improve the care and treatment of older-aged patients through evaluation of tolerance and response to standard, experimental, newly-designed anti-cancer agent regimens independent of, and in conjunction with, multimodality interventions in the context of geriatric pharmacology. It encourages

the extramural research communities in cancer and geriatric pharmacology to combine expertise and apply the knowledge bases of both disciplines to research initiatives relevant to older cancer patients.

Clinical studies relevant to this pharmacology initiative promote two major areas of investigation: 1) Studies to assess the age-dependent differences that influence drug efficacy and adverse drug effects used to treat the tumors that disproportionately affect the elderly. This includes the parameters of drug absorption, distribution, metabolism, and excretion as well as age-host and drug interactions. Alterations in immune function and cell cycle kinetics may also affect the pharmacodynamics of the therapeutic drugs. What influence does age have on these physiologic factors and the proposed therapeutic intervention? 2) Cancer site-specific studies that confront and deal with the multiple health problems inherent in older persons diagnosed with a malignancy. How are these conditions and their multiple pharmacy needs managed in the context of cancer treatment planning? What impact do co-existing health problems have on clinical trial enrollment?

Selected areas for studies are listed. Grant applications are not limited to these specific areas.

--Studies on how anti-cancer agent effects are modified by aging processes with attention to dosage, adverse reactions, drug-drug interaction, drug-age interaction, changes in body composition, organ, and immune function, and the older person's own use of medications (prescribed and over the counter).

--Prospective studies that emphasize the entry of older-aged patients into cancer treatment protocols that will evaluate the independent effects of age-related factors. These studies may involve chemotherapy, biologic therapy, surgery, radiation therapy, and multimodality treatment interventions.

--Phase IV trials may be developed to address ways to improve therapeutic management of older patients.

--Pharmacokinetics and pharmacodynamics modeling of selected anti-cancer agents and patient response applied to chemotherapy and biologic therapy questions pertinent to elderly patients.

--Age-associated toxicity effects. Mucositis, cardiotoxicity, nephrotoxicity, myelotoxicity, and neurotoxicity.

--Age-associated pharmacodynamic effects. Mechanisms of antitumor drug resistance and repair, markers of angiogenesis and related events, immune responsiveness.

--Explore differences in the pharmacokinetics and pharmacodynamics of chemotherapeutic and biologic antitumor agents between older and younger patients and the potential mechanisms for these differences.

--Studies that characterize the inadmissible elderly patients to research protocols (e.g., physical incapacity from other medical conditions; family/patient decisions; memory loss; depression; cognitive function; lack of social support or transportation) that include data on treatment administered in the clinical setting outside the protocol involvement.

--Development of methods to evaluate performance status of older patients regarding preexisting diseases or conditions as prognostic indicators for drug sensitivity and dose intensity.

--Development of leads for research on cancer pharmacology in older patients from extant databases.

Inquiries: Rosemary Yancik, Geriatrics Program, NIA, 7201 Wisconsin Ave Suite 3E327 MSC 9205, Bethesda, MD 20892-9205. Tel: 301/496-5278, fax: 301/402-1784, email: YancikR@exmur.nia.nih.gov

Diane Bronzert, DCTD, NCI, 6130 Executive Blvd Suite 734 MSC 7432 Bethesda, MD 20892-7432. Tel: 301/496-8866, fax: 301/480-4663, email: Bronzertd@ctep.nci.nih.gov

In Brief:

List Of Cancer Survivors Underway; AACR Awards

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has a personal story of coping with the disease. Schimmel was diagnosed with breast cancer 15 years ago while attending UCLA. Nominations may be mailed to Vital Options, PO Box 19233, Encino, CA 91416-9233; faxed to 818-788-5260; or e-mailed to list@vitaloptions.org. . . . . **AMERICAN ASSOCIATION** for Cancer Research has awarded seven postdoctoral and clinical research fellowships to young scientists. Recipients are **Richard Reilly**, Johns Hopkins Univ. School of Medicine; **Andrew Joe**, Columbia Univ./Columbia Presbyterian Medical Center; **Paul Boucher**, Univ. of Michigan; **Chung-Tsen Hsueh**, Memorial Sloan-Kettering Cancer Center' **Stephen Buck**, Johns Hopkins School of Medicine; **John Timmerman**, Stanford Univ. Medical Center; and **John Frangioni**, Beth Israel Deaconess Medical Center, Harvard Medical School. . . . **WILLIAM BLOOMER**, chairman of radiation medicine at Evanston Northwestern Healthcare and professor of radiology at Northwestern Univ., has been awarded the gold medal of the American College of Radiation Oncology. . . . **DONALD TRUMP**, deputy director for clinical investigations at the Univ. of Pittsburgh Cancer Institute, has received two awards totaling $180,000 from CapCure and the Mary Hillman Jennings Foundation for his research on the role of vitamin D and its potential for prevention of prostate cancer.