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THE CLINICAL CANCER LETTER

Cancer research news for clinicians

American Association for Cancer Research:

Diet and Cancer Risk Explored In Studies Presented At AACR Annual Meeting

ORLANDO—Two case-control studies presented at the annual meeting of the American Association for Cancer Research compared specific eating habits of healthy individuals to those with prostate and bladder cancers to assess the relationship between dietary factors and incidence of disease. Both found inverse associations between diet and cancer risk.

A third case-control study of breast cancer found that the effects of

(Continued to page 2)

Clinical Trials:

Gynecologic Oncology Group To Conduct Phase III Trial of Xyotax For Ovarian Cancer

Cell Therapeutics Inc. and the Gynecologic Oncology Group have signed a clinical trials agreement through which the GOG will sponsor and conduct a phase III clinical trial of XYOTAX in patients with ovarian cancer.

This represents the first time the GOG will submit an IND and use the FDA's SPA process for the review of a proposed pivotal trial.

"We believe the potential benefit of XYOTAX to our patients' quality of life is consistent with the GOG's desire to provide less toxic, more effective therapies for patients with gynecologic cancers," said Larry Copeland, vice chairman of the GOG and chairman of the Department of Obstetrics and Gynecology at the James Cancer Hospital at Ohio State University. "We've been encouraged by our initial interactions with the FDA regarding a pivotal XYOTAX trial and should be positioned within the next several weeks to submit our IND and the phase III protocol under the FDA's SPA procedure—a first for the GOG."

The trial will investigate the safety and efficacy of XYOTAX, administered over about 10 minutes once a month for 12 months, compared to no maintenance therapy to prolong progression free survival and overall survival in women with ovarian cancer who have achieved a complete remission following standard front-line chemotherapy. The phase III trial is expected to enroll approximately 1500 patients. A standard formulation of Taxol will also be investigated as a third treatment arm. The study will assess potential differences in toxicity, tolerability and patient quality of life between treatment groups. These differences will constitute secondary

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AACR Meeting: Role of Diet In Cancer Risk Explored

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genetics were modified greatly by dietary antioxidants.

Higher serum alpha-tocopherol and gamma-tocopherol concentrations are associated with lower prostate cancer risk: Two forms of vitamin E, alpha- and gamma-tocopherol, appear to lower the risk of prostate cancer by as much as 53 percent and 39 percent, respectively, based on the findings of a team of scientists from the National Cancer Institute, the Fred Hutchinson Cancer Research Center in Seattle, and the National Public Health Institute of Finland.

The researchers, led by Stephanie Weinstein and Demetrius Albanes the NCI Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, drew their subjects from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study cohort of 29,133 Finnish men, aged between 50 and 69 years.

From that group were selected 100 men with prostate cancer and 200 without, to determine whether there exists an association between higher levels of vitamin E circulating in the blood stream and lower risks of prostate cancer. The ATBC Study previously demonstrated a 32-percent reduction in the rate of prostate cancer among men who took 50 mg of alpha-tocopherol per day for a period of 5 to 8 years.

Since the baseline value for serum levels of alpha-tocopherol and gamma-tocopherol in this study came from blood drawn before men in the ATBC trial started taking any pills, use of vitamin E supplements was a factor only if the participants had been taking them already. Ten percent had, leaving 90 percent whose serum levels of alpha-tocopherol and gamma-tocopherol could be attributed exclusively to dietary intake.

In keeping with earlier findings, the men who were randomized to receive a vitamin E supplement as part of the ATBC trial and who had the highest serum vitamin E levels at baseline displayed the lowest risk of prostate cancer.

"Nuts and seeds, whole grain products, vegetable oils, salad dressings, margarine, beans, peas and other vegetables are good dietary sources of vitamin E," Weinstein said.

"Even though gamma-tocopherol is by far more prevalent in U.S. diets, alpha-tocopherol is found in greater concentrations in the blood. That is at least in part because a protein in the liver called alpha-tocopherol transfer protein preferentially binds alpha-tocopherol and secretes it into the plasma."

Weinstein further noted that one principal dietary difference between Finns and Americans is the type of cooking oils used. "The Finns generally eat more canola oil, while Americans favor corn or soybean oils," she said. "Canola oil is richer in alpha-tocopherol and offers the added benefit of being lower in saturated fat."

To achieve optimum serum levels of alpha- and gamma-tocopherols, Weinstein recommends following the Dietary Guidelines for Americans, published by the U.S. Department of Agriculture and the U.S. Department of Health and Human Services. The guidelines call for eating more fruits, vegetables and whole grains, and fewer fats and sugars.

Intake of vitamin E (2-R isomers of alpha-tocopherol) and gamma-tocopherol in a case-control study and bladder cancer risk: Consuming vitamin E (alpha-tocopherol) lowers the risk of bladder cancer, according to the findings of a case-control study led by Xifeng Wu, of the University of Texas M.D. Anderson Cancer Center in collaboration with researchers at Texas Woman's University.

M.D. Anderson research dietician Ladia M. Hernandez, John Radcliffe, of Texas Woman's University, and several epidemiologists at M.D.

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Anderson evaluated the association between intake of vitamin E (2-R isomers of alpha-tocopherol) from dietary sources only, from diet and supplements combined, and from dietary gamma-tocopherol.

Personal interviews were conducted with 468 bladder cancer cases and 534 healthy, cancer-free controls, using a modified version of NCI's Health Habits History Questionnaire. The questionnaire was modified to incorporate supplements use and ethnic dishes commonly consumed in the Houston area. Radcliffe developed a database with values assigned to the tocopherol content of foods, based on published values and values for such foods as cornbread, French fries and tomatillos, determined specifically for the study. He found almonds, spinach, mustard greens, green and red peppers and sunflower seeds to be excellent sources of a-tocopherol.

"High intake of vitamin E from dietary sources alone was associated with a 42 percent reduced risk of bladder cancer, whereas high intake of vitamin E from dietary sources and supplements combined reduced the risk by 44 percent," Hernandez reported.

As NCI's Weinstein also pointed out, gamma-tocopherol is the most common tocopherol in the U.S. diet. Even so, its effect on cancer risk had never before been tested in a case-control study. Hernandez and her colleagues found gamma-tocopherol to have no protective effect against bladder cancer.

Catalase genotype, dietary antioxidants, and breast cancer risk: In the first study to evaluate catalase (CAT) genotypes and breast cancer, researchers at Roswell Park Cancer Institute found that women with the most common genotype for reducing oxidative stress are at a reduced risk of developing breast cancer.

Further, they can diminish their breast cancer risk even more by including ample fruits and vegetables in their diets.

Fruits and vegetables are known to reduce the risk of some cancers through their antioxidant properties; that is, by inhibiting reactive oxidant species. These free radicals form naturally in the course of cell respiration and metabolism, but have been linked with disease-causing damage to tissue and changes in DNA that can lead to malignancies.

While this oxidative stress is considered to be a major causative factor for breast cancer, prominent research including the Nurses Health Study has shown no link between increased consumption of fruits and vegetables and decreased breast cancer risk. Because the evidence on whether fruits and vegetables reduce the risk of breast cancer is not clear, the investigators from Roswell Park thought that effects might be limited to women with specific genotypes related to protection from oxidative stress.

Jiyoung Ahn, a pre-doctoral research associate in the department of epidemiology at Roswell Park, and a Ph.D. student in the division of nutritional sciences at Cornell University, considered the fact that *CAT* is one of the most effective enzymes in the body for reducing oxidative stress. It converts hydrogen peroxide into water and oxygen, thus neutralizing reactive oxygen species. Ahn wondered if higher levels of the endogenous antioxidants that course through the human blood stream naturally—like those resulting from the *CAT* C (CC) allele—might provide some degree of antioxidant protection against breast cancer, and if the risk might be further diminished by the consumption of fruits, vegetables and specific antioxidants.

Working with her academic advisor, Christine Ambrosone, chairwoman of the Roswell Park department of epidemiology, Ahn evaluated this hypothesis in a population-based, case-control study of 1,037 women with breast cancer and 1,086 healthy subjects in Nassau and Suffolk Counties, N.Y., conducted originally by Marilie Gammon and colleagues. Each woman was interviewed at home to assess suspected breast cancer risk factors over the course of her lifetime, and administered the Block food frequency questionnaire to determine dietary intake the preceding 12 months.

The women were genotyped, with the most common genotype the *CAT* C (CC), present in a little more than 60 percent of the cases and the controls. A CT polymorphism exists in the (*CAT*) gene in about 33 percent of participants, and all others—some four percent—have the TT genotype.

Women with the CC genotype and a diet rich in fruits and vegetables had a 30 percent reduced risk of breast cancer. There was only a five percent lower risk in women with the CC genotype who ate very few fruits and vegetables.

"With so many women having the CC genotype," said Ahn, "our study potentially has a very important public health impact. Of course, none of us knows our exact genetic make-up, but since eating a diet high in fruits and vegetables is known to contribute to a healthy lifestyle anyway, women can consider it a viable means of reducing their breast cancer risk, as well."

Regular Exercise May Prevent Cancer, Improve Survival

ORLANDO—Regular exercise may help prevent certain cancers and improve the odds of cancer survival, according to studies presented at the annual meeting of the American Association for Cancer Research.

Two studies report a strong correlation between such ordinary activities as walking or performing household chores and reduced risk of endometrial and breast cancers, and between walking and improved rates of breast cancer survival. Another demonstrates that moderate exercise decreased the levels of a blood marker that predicts lower survival from several types of cancer among high-risk, obese individuals. The research was presented here today at the 95th Annual Meeting of the American Association for Cancer Research.

Physical activity and endometrial cancer risk: Regular exercise, as well as routine activities such as walking and household chores, may reduce a woman's risk of endometrial cancer by as much as 30 to 40 percent, according to researchers from the Vanderbilt University Medical Center and the Shanghai Cancer Institute.

Charles Matthews, of Vanderbilt, and his colleagues evaluated 832 women with endometrial cancer, aged 30 to 69 years, identified through the Shanghai Cancer Registry. The control population, matched according to age, was randomly selected from female residents of Shanghai.

The women were asked about the amount of walking and cycling for transportation, intentional exercise and household activity in which they engaged as adolescents and as adults. Lifetime occupational activity was also evaluated.

Women who reported exercise participation in both adolescence and adulthood were 30 to 40 percent less likely to develop endometrial cancer than women who reported no exercise in either life-period. Common activities, including household chores and daily walking, were also found to reduce risk by about 30 percent. Reductions in risk were evident for women who reported walking for 60 minutes each day compared to women reporting less than 30 minutes of walking per day; likewise for women who reported four or more hours per day of household activity, compared to women reporting two hours or less each day.

Engaging in higher levels of overall physical activity appeared to minimize some of the adverse effects of body weight on endometrial cancer risk. Neither cycling nor occupational activity appeared to influence endometrial cancer risk in this study.

"In recent years, we have accumulated strong evidence that an active lifestyle can reduce the risk of colon and breast cancer; now we are finding that physical activity may also reduce risk of endometrial cancer" said Matthews, the lead author of this report.

"We were particularly pleased to see the beneficial effect on endometrial cancer risk of more accessible and lower intensity forms of activity like walking for transportation and doing household chores, as well as intentional exercise," he added. "Our results support the idea that the risk of cancer can be reduced by maintaining an active lifestyle."

Physical activity and survival after breast cancer diagnosis: Researchers from Brigham and Women's Hospital and Harvard University tested the hypothesis that physical activity increases survival rates among women with breast cancer.

"We already knew that exercise improves the quality of life after a breast cancer diagnosis, but little is known about how physical activity affects survival," said lead investigator Michelle Holmes.

Holmes and her team drew on participants in the Nurses' Health Study, reviewing data on women with stages I, II, and III breast cancer, diagnosed between 1984 and 1996. In that study, leisure-time physical activity is measured in metabolic equivalent task hours per week (met-hours/week—one met is the energy expenditure and caloric requirement at rest. One hour of walking represents three met-hours of physical activity.)

The researchers looked specifically at exercise beginning two years after diagnosis, in order to avoid inclusion of women undergoing treatment. The cohort of 2,296 women were followed from 1986 until either their death from breast cancer or June 2002, whichever came first.

Taking into account the stage of disease, obesity and other factors, the relative risk of death from breast cancer was decreased with every level of physical activity compared with being sedentary. The risk of death from breast cancer was 19 percent less among women who undertook 3-8.9 met-hours/week of exercise; 54 percent less for 9-14.9 met-hours/week; 42 percent less for 15-23.9 met-hours/week; and 29 percent less for 24 or more met-hours/week of

recreational exercise.

"We were able to show that even a moderate amount of physical activity improved the odds of surviving breast cancer," Holmes said. "It is especially heartening for women recovering from breast cancer to know that the benefit is as readily accessible as walking for 30 minutes on most days of the week."

Effect of a yearlong exercise intervention on markers of inflammatory response among postmenopausal women: Another approach to the association between exercise and cancer survival and prevention was presented by researchers from the Fred Hutchinson Cancer Research Center, led by Cornelia Ulrich.

C-reactive protein (CRP) and serum amyloid A (SAA) are signals for inflammation that have been associated with cancer risk and survival. Knowing that these biomarkers often are elevated among the overweight, the team investigated the effects of a moderately intense, yearlong exercise program on CRP and SAA.

The study population consisted of 114 postmenopausal, overweight (body mass index greater than 24) and sedentary women, ages 50 to 75. About half of these performed moderate physical activity 45 minutes per day, five days a week, for one year, while the other half participated in weekly stretching exercises. The concentrations of CRP and SAA in their blood were measured at the beginning and the end of the test period.

"Among obese women, those with a body mass index of 30 or higher, concentrations of CRP declined steadily over the course of the year from a baseline of 0.40 milligrams per deciliter to 0.32 milligrams," Ulrich said. "This effect of exercise on inflammatory markers may help to explain in part the associations observed between increased physical activity and reduced risk for cancer and other chronic disease."

Cancer Prevention:

Cancer Deaths In Black Men Could Drop By Cutting Tobacco

The overall cancer death rate for African-American males would drop by nearly two-thirds without any other intervention if their exposure to tobacco smoke was eliminated, a new study suggests.

"African-American men have had the highest cancer burden of any group in this country for decades," said study author Bruce Leistikow, associate professor of epidemiology and preventive medicine at University of California, Davis, School of Medicine and Medical Center. "This study demonstrates, for the first time, that this excess cancer burden can be clearly linked to smoking. Smoke exposure appears responsible for African-American males' high overall cancer mortality rates, not just their lung cancers."

The study is published in the May issue of the journal Preventive Medicine.

Leistikow found data suggesting that tobacco smoke exposure is responsible for more than half the non-lung cancer death rate in African-American males and up to two thirds of their overall cancer death rate.

"This means that if black male smoking exposures fall dramatically, that alone is likely to erase the great majority of their cancer burden," said Leistikow. "Going back to the low black male cancer burdens seen before the cigarette epidemic appears possible. Indeed, New York and, less so, California appear to be well on their way there."

Leistikow used lung cancer death rates as a measure of smoke exposure. He then analyzed the correlation between annual smoke exposure and non-lung cancer death rates for black males in the U.S. for 1969-2000. Throughout this 31-year period, he found that the non-lung cancer death rate closely shadowed the smoke exposure rate. Non-lung cancer mortality rose about 34 percent among black males during the first two decades of the study period, paralleling a steep rise in smoke exposure. From 1990 through 2000, the mortality rate dropped 11 percent as smoking declined.

"During two decades of a steep rise, and a subsequent decade of steep fall, U.S. black male smoke exposures and non-lung cancer death rates have moved in near-perfect lockstep," hesaid.

African-American male cancer burdens first surpassed white levels in the 1950s. Their cancer mortality rate excess peaked in 1995, at 44 percent above the rate for white males.

According to the Centers for Disease Control and Prevention, the overall age-adjusted cancer death rate for African-American men is 330.9 deaths per 100,000 individuals, compared to 239.2 for white men. In New York, the overall cancer death rate for black males is 256.7. In California, it's 309.3.

In 1950, the overall cancer mortality rate was 178.9 for black males versus 210 for white males.

Breast Cancer:

Surgery Lowers Risk By 90% In Women With Gene Mutations

A study led by the Abramson Cancer Center of the University of Pennsylvania found that prophylactic double mastectomy can lower the risk of developing breast cancer by 90 percent in women genetically predisposed to the disease.

This is the first study to quantify the risk reduction for this procedure in women who carry mutations in BRCA1 and BRCA2 linked to breast and ovarian cancer.

"Now that we have quantified the benefit of a double mastectomy for reducing the chances of breast cancer, women in this high-risk group can make a better-informed decision about having breast surgery in addition to other forms of prevention, such as regular screening or other preventive surgeries, including ovary removal," said Timothy Rebbeck, of the center's Cancer Epidemiology and Risk Reduction Program and lead author of the study that appeared in the Journal of Clinical Oncology March 15.

The Prevention and Observation of Surgical Endpoints study followed 483 at-risk women from the U.S., Canada, United Kingdom, and the Netherlands for over six years. Breast cancer was diagnosed in two of 105 women (1.9 percent) who had double mastectomies. The occurrence of breast cancer was much greater in the control group, with 184 of 378 women (48.7 percent) developing breast cancer.

Study results also confirmed a large risk reduction for breast cancer (95 percent) for women who also had their ovaries removed.

Chemoprevention:

Proteomics Used To Find Predictor Of Response In FAP

Using new technology associated with the study of proteins, or proteomics, scientists at the National Cancer Institute have made a step toward predicting which people with familial adenomatous polyposis (FAP), an inherited condition that often leads to colon cancer, will respond to the prevention drug celecoxib.

This study, published in the April 15 issue of the journal Cancer Research, is the first to report using proteomics techniques to find a possible predictor of response in a chemoprevention trial.

Iqbal Ali, in the NCI Division of Cancer Prevention, and collaborators examined protein patterns among people who had been given celecoxib in a chemoprevention clinical trial in which the drug reduced the number of colon polyps characteristic of patients with FAP. Celecoxib inhibits an enzyme called cyclooxygenase 2, which has been associated with various cancers in addition to colon cancer. These clinical trial results were reported in June 2000 and led to approval by the Food and Drug Administration of celecoxib as a chemoprevention agent for people with FAP.

Not everyone in the 2000 study taking celecoxib experienced polyp reduction, however. Ali's group, employing a new proteomics technique, was able to distinguish the people who responded to the drug from those who did not.

Ali's laboratory used serum from the blood of 55 people who had participated in the celecoxib prevention trial. Serum contains tens of thousands of proteins. Using a specialized form of mass spectroscopy as a proteomics tool, the patients' proteins were separated and reported as a series of peaks. The pattern of protein peaks can be used to differentiate groups of patients.

The scientists analyzed blood obtained at the beginning of the prevention study—before participants received any celecoxib—and compared the pattern of protein peaks from the patients who didn't respond to the drug to the protein pattern of those who had a good response. One particular protein peak occurred in the serum of those people who did not benefit from the drug. The same protein peak was absent in those people whose polyps were reduced.

Although the technique has not been tested enough to be used in the clinic to identify those with FAP who will respond to celecoxib, the scientists are refining the technique for possible future clinical use.

"This study is a promising first step in using proteomics for personalized colon cancer prevention," said Ali. "A lot more work is needed before patients' responses to specific chemopreventive drugs can be reliably predicted."

In addition to predicting who responded to celecoxib, the scientists also used the proteomics technique to look at how protein patterns in each patient changed after being given the drug. They found that of thousands of possible proteins, only a few protein peaks were changed significantly in all patients following administration of celecoxib. The researchers are now trying to identify these proteins to learn more about how the drug works.

Operative Laparoscopy Safe For Endometrial Cancer

By Lawrence M. Prescott

SAN DIEGO—Results from a retrospective review point out that laparoscopy with CO_2 pneumoperitoneum can be used safely with diagnostic and/or therapeutic intent in patients with stage III endometrial cancer, according to a presentation at the annual meeting of the Society of Gynecologic Oncologists.

"The use of operative laparoscopy with CO_2 pneumoperitoneum does not appear to affect the survival for patients diagnosed with advanced endometrial cancer," said Ram Eitan, fellow, gynecology service, department of surgery, Memorial Sloan-Kettering Cancer Center. "Furthermore, the presence of extrauterine disease does not appear to be a contradiction to laparoscopy."

Most patients with endometrial cancer are diagnosed at an early stage, such as stage I or II, Eitan said. For these patients, the mainstay of treatment is surgery. Laparoscopy is frequently used for the treatment and staging of apparent early-stage endometrial cancer but the effect of laparoscopy and CO_2 pneumoperitoneum on survival in endometrial cancer and, especially, in advanced-stage disease is not known. A study, therefore, was carried out to evaluate the effect of laparoscopy with CO_2 pneumoperitoneum on survival in patients with advanced endometrial cancer.

A chart review was conducted from a prospectively acquired database of all patients treated at MSKCC for endometrial cancer between November 1995 and June 2001, Eitan said. Information regarding demographics, surgical procedure, staging, grading, pathology, and survival was collected. Differences between groups were calculated using the t-test for continuous variables.

Overall, 468 patients had surgery for endometrial cancer during the study period, Eitan said. Of these, 310 patients had laparotomy performed and 158 patients had laparoscopy with CO_2 pneumoperitoneum as their primary surgical procedure, with 140 patients having a laparoscopically assisted vaginal hysterectomy, BSO, and staging. Of the entire patient population, 87 patients were found to have advanced stage disease, with 42 stage III and 29 stage IV. In the patients with advanced disease, 71 had a laparotomy and 16 had laparoscopy as their primary surgical procedure. Age, histology (adenocarcinoma, serious carcinoma, clear cell carcinoma) and menopausal status were similar in both study groups.

Survival was evaluated for the stage III group separately and for stages II and IV combined, Eitan said. Median survival rates for 56 stage III patients were 43 months for the 42 patients who underwent laparotomy and 37 months for the 14 stage III patients who underwent laparoscopy with CO_2 pneumoperitoneum. Median survival rates for the 87 stage III and IV patients were 37.3 months for the 71 patients who underwent laparotomy and 37.6 months for the 16 patients who had laparoscopy with CO2 pneumoperitoneum.

Adjuvant intraperitoneal radioactive phosphorus and vaginal brachytherapy

Findings from a prospective phase II study strongly suggest that adjuvant intraperitoneal radioactive phosphorous (^{32}P) and vaginal brachytherapy be used as adjuvant treatment in patients with uterine papillary serous carcinoma (UPSC) and clear cell carcinoma, according to Achilles Fakiris, clinical instructor in gynecology oncology, Indiana University School of Medicine.

"Adjuvant therapy for UPSC and clear cell carcinoma with intraperitoneal radioactive phosphorous and vaginal brachytherapy after adequate surgical staging and maximal cytoreduction is well tolerated and effective," Fakiris said. "Further study on a larger scale is warranted."

Uterine papillary serious carcinoma and clear cell carcinoma are aggressive histologic subtypes which comprise up to 10% of all endometrial adenocarcinomas. They are associated with a poor prognosis and similar patterns of spread, both having a propensity for peritoneal dissemination. Complete surgical staging is mandatory for all patients. Unfortunately, even for early stage disease after aggressive surgical staging, freedom from relapse is difficult to predict, and there is no agreement regarding the optimal adjuvant therapy.

The Hoosier Oncology Group conducted a phase II study to evaluate the role of adjuvant intraperitoneal radioactive ^{32}P administration in addition to vaginal brachytherapy in patients with comprehensively staged UPSC and CCC. Eligible patients were those with UPSC and CCC who had undergone complete surgical staging, Fakiris said. A distribution study using $Tc^{99}m$ was performed prior to the intraperitoneal administration of ^{32}P, to ensure adequate distribution

of the radioisotope throughout the intraperitoneal surfaces. Intraperitoneal ^{32}P was administered within 8 weeks of surgery. Vaginal brachytherapy was administered as either a high dose of 2100 cGy in 3 fractions, as 700 cGy per fraction to 0.5 cm depth from the vaginal surface, or a low dose to 6500 cGy in 1 to 2 fractions, prescribed to the vaginal surface.

From 1997 to 2003, 21 evaluable patients were entered and completed the treatment. The median followup was 39.6 months. Acute toxicity was minimal and no patients had grade 3 or 4 complications related to their adjuvant treatment. Five patients had recurrent disease, 2 initially relapsing intraperitoneally, 2 recurring in the distal vagina and 1 had a scar recurrence. After the two initial recurrences in the distal vagina, a decision was made to treat the entire length of the vagina with intracavity brachytherapy. No additional vaginal recurrences have been observed.

Overall, three patients have died of their disease. Another patient with no evidence of disease at last followup over 2 years died of pancreatic carcinoma. For all 21 patients, the two-year overall survival, cause-specific survival, and disease-free survival were 89.2%, 89.2%, and 79.7% respectively. If only the 17 stage I and II patients are considered, the respective two-year survivals are 93.3%, 93.3%, and 87.1%, while for the four patients with stage III or IV disease, the respective two year survivals are 75%, 75%, and 50%.

Clinical Trials:

GOG To Lead Phase III Trial Of Xyotax for Ovarian Cancer

(Continued from page 1)

endpoints of the trial. The trial design is similar to one conducted by the National Cancer Institute, Southwest Oncology Group, and GOG testing the efficacy of maintenance paclitaxel. Results of this study were published in the July 2003 issue of the Journal of Clinical Oncology.

"The XYOTAX study will answer a critical question: Does maintenance therapy prolong overall survival as well as PFS in patients with advanced ovarian cancer after first-line therapy?" said James Bianco, president and CEO of Cell Therapeutics. "Paclitaxel maintenance therapy is not considered standard of care for front-line ovarian cancer patients despite the maintenance study that showed that paclitaxel maintenance therapy significantly improved PFS. This is largely because of the toxicities observed with monthly paclitaxel maintenance and the fact that the prior study was stopped before it had adequate power to demonstrate a benefit in overall survival. With an enrollment target of 1500 patients the XYOTAX trial is designed to have adequate power to demonstrate the potential to improve PFS and OS and to provide a better tolerated alternative to standard paclitaxel with less impact on a patient's quality of life. The trial is consistent with our goal of making cancer a chronic disease."

According to a recent market survey, approximately 60 percent of patients (15,240 in 2003) receive surgery followed by chemotherapy for newly diagnosed advanced ovarian cancer. The standard front-line regimen consists of paclitaxel (175mg/m2) and carboplatin (AUC 6) for up to six cycles. Approximately 70 percent of patients will achieve a complete response with front-line therapy and would be eligible for treatment with monthly maintenance XYOTAX therapy for up to 12 months.

XYOTAX (Paclitaxel poliglumex) is a pharmaceutical that links paclitaxel to a biodegradable polyglutamate polymer. This polymer technology results in a new chemical entity, designed to selectively deliver higher and potentially more effective levels of active chemotherapeutics to tumors.

Protocols Approved By NCI

The National Cancer Institute's Cancer Therapy Evaluation Program Approved the following clinical research studies last month. For further information about a study, contact the principal investigator listed.

Phase I

Phase I Trial of Bortezomib and Flavopiridol in Patients with Recurrent or Refractory Indolent B-cell Neoplasms. NSC Medical College of Virginia, protocol 6413, Grant, Steven, phone 804-828-5211.

Phase II

Phase II Study of CCI-779 in B-cell Lymphoma and CLL. University of Chicago, protocol 6199, Van Besien, Koen, phone 773-702-6696.

Adjuvant Chemo-Radiotherapy with Combination of Cisplatin and Docetaxel after Complete Resection of Locally Advanced (Stage III and IV) Squamous Cell Carcinoma of the Head and Neck. Southwest Oncology Group, Coltman, Charles, phone 210-616-5580.