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THE CLINICAL CANCER LETTER

Cancer research news for clinicians

Angiogenesis Inhibitor In Phase III Trials For Metastatic Colorectal Cancer

An experimental agent PTK787/ZK 222584 being developed by Novartis and Schering AG has entered phase III clinical trials for metastatic colorectal cancer.

The trials are designed to evaluate the safety and efficacy of PTK787/ZK 222584 in combination with first- and second-line chemotherapy for patients with metastatic colorectal cancer.

PTK787/ZK 222584 is an oral angiogenesis inhibitor that potently inhibits vascular endothelial growth factor (VEGF) receptor tyrosine

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Clinical Trials:

Provenge Prolonged Prostate Cancer Survival By Seven Months, Study Finds

Preliminary results of a phase III trial of Provenge immunotherapy for prostate cancer indicate that patients taking Provenge survived 7 months longer than patients randomized to the placebo group.

Dendreon Corp. released the preliminary survival data and final audited date from D9901, a randomized, double blind, placebo-controlled trial. The results were scheduled to be presented at the Prostate Cancer Foundation (formerly CaP CURE) Tenth Annual Scientific Retreat, in Washington, D.C., Sept. 19-21. The conference was postponed due to hurricane Isabel.

The Provenge D9901 trial was designed to measure time to disease progression and time to development of disease-related pain in men with androgen independent prostate cancer.

Patient survival was also measured. Preliminary analysis of survival data show a median survival of 26.3 months in the patients randomized to the Provenge treated group compared to 19.3 months in patients randomized to the placebo group who never received active therapy—a survival difference of 7 months.

Seventy five percent of patients who were randomized to placebo and then had progression of their disease went on to receive active therapy in a crossover salvage protocol that accompanied the D9901 trial. The median survival in the patient population who received salvage Provenge was 23.9 months, a survival difference of 4.6 months compared to placebo.

Of the 127 men enrolled in the trial between January 2000 and October 2001, over half (67 men) are still alive, with more than 90 percent having received treatment with Provenge, either as initial treatment or as

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Phase III Trials Testing Angiogenesis Inhibitor

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kinases, important enzymes in the formation of new blood vessels that contribute to tumor growth and metastasis.

The CONFIRM 1 (Colorectal Oral Novel Therapy for the Inhibition of Angiogenesis and Retarding of Metastases in First-line) trial will study the potential progression-free and overall survival benefit of once daily oral treatment with PTK787/ZK 222584 in combination with oxaliplatin/5-fluorouracil/leucovorin (FOLFOX-4 regimen) compared to FOLFOX-4 with placebo in previously untreated patients with metastatic colorectal cancer.

The CONFIRM 2 (Colorectal Oral Novel Therapy for the Inhibition of Angiogenesis and Retarding of Metastases in Second-line) trial will study the potential survival benefit of once daily oral treatment with PTK787/ZK 222584 in combination with the FOLFOX-4 regimen compared to FOLFOX-4 with placebo in patients with metastatic colorectal cancer who have progressed after irinotecan-based first-line therapy.

"There is a pressing clinical need to pursue the development of new cancer therapies for metastatic colorectal cancer," said Gregory Burke, senior vice president, Global Head Development, Novartis Oncology. "By restricting the blood supply to these tumors, the angiogenesis inhibitor PTK787/ZK222584 represents a novel approach to cancer treatment. If the data continue to be positive, addition of this novel compound to standard chemotherapy could represent a new treatment option for patients with metastatic colorectal cancer."

CONFIRM 1 is scheduled to enroll about 1,090 patients with previously untreated metastatic colorectal cancer, while CONFIRM 2 is seeking approximately 830 patients with metastatic colorectal cancer who have progressed after irinotecan based first-line therapy. More than 200 sites worldwide will participate in these trials.

PTK787/ZK 222584 treatment has been generally well tolerated in the ongoing clinical trials. The most frequently reported adverse events were nausea (47%); fatigue (39%), vomiting (36%), and dizziness (34%) and the majority of these were mild to moderate. The adverse event profile for the group of patients treated with PTK787/ZK 222584 in combination with FOLFOX-4 was generally similar to that of the FOLFOX-4 regimen alone.

For information on participating in the study, patients in the U.S. may call 800-340-6843.

NCCN Updates Myeloma Clinical Practice Guidelines

The National Comprehensive Cancer Network, an alliance of 19 of the world's leading cancer centers, has updated its Multiple Myeloma Clinical Practice Guidelines.

The NCCN panel of oncology experts has added bortezomib (Velcade, Millennium Pharmaceuticals Inc.) to its listing of chemotherapeutic agents that are considered appropriate for patients with progressive or refractory multiple myeloma who have previously been treated with conventional dose chemotherapy alone or followed by high dose chemotherapy and stem cell transplant.

Another update is the inclusion of the combination of thalidomide (Thalomid, Celgene Corp.) and dexamethasone on the list of options for the primary treatment of disseminated disease. Thalidomide had previously been recommended as an approach to managing progressive or refractory multiple myeloma.

NCCN Clinical Practice Guidelines in Oncology are available free of charge on CD-ROM, by calling 215-690-0300. The guidelines can also be found at www.nccn.org.

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Clinical Trials:

Provenge Results In Longer Prostate Cancer Survival

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part of the salvage protocol. Final survival data from D9901 is anticipated to be available in late 2004 to early 2005.

The final audited results from the D9901 trial confirm the previously reported preliminary results, the company said. Comparison of the Provenge treated group to placebo group using the Kaplan-Meier method revealed a clinical benefit, as measured by a delay in time to disease progression, in the Provenge treated group ($p = 0.061$) that closely approached, but did not achieve, the pre-specified endpoint of the study ($p = 0.05$). The p value previously reported in the preliminary analysis was ($p = 0.085$).

Final audited results from the trial also confirmed the significant clinical benefit of delay in time to disease progression from Provenge treatment for men with androgen independent prostate cancer with a Gleason score of 7 or less ($p = 0.001$), an improvement from that previously reported in the preliminary analysis ($p = 0.002$).

The probability of remaining free of cancer-related pain while on the study was more than two times higher ($p = 0.016$), preliminarily reported as ($p = 0.019$), than for patients treated with placebo. Treatment was generally well tolerated, with mild infusion-related fevers and chills the most common adverse events.

Provenge is currently in a pivotal double blind placebo-controlled phase 3 trial, D9902B, seeking to confirm previous results that indicate the product may delay progression of disease and the development of disease-related pain.

Dendreon has received a Fast Track designation for Provenge from the FDA in addition to a positive assessment under the Special Protocol Assessment provision indicating that D9902B may serve as the basis for a Biologics License Application for Provenge.

To be eligible for the current Provenge D9902B study, patients must have metastatic prostate cancer that has progressed following hormone therapy and have a Gleason score of 7 or less. Patients must also be free of cancer-related pain.

Further information on Provenge clinical trials is available at www.dendreon.com.

Wilmot Researchers Study Combination for Lymphoma

Researchers at the James P. Wilmot Cancer Center have joined a national effort to find a companion to Rituxan that could broaden its effectiveness in combating lymphoma.

Rituxan is being combined with another antibody, IDEC-114, to treat people with relapsed follicular lymphoma.

In the last five years, Rituxan has become a standard treatment for lymphoma. Rituxan was the first monoclonal antibody used to deliver toxins or radioactive material to destroy cancer cells, approved for cancer therapy. It is prescribed alone, or in combination with chemotherapy.

"This combination shows promise in the few patients that have been treated with it already, with minimal side effects," said Jonathan Friedberg, of the Wilmot Cancer Center Lymphoma Program. "This may be a significant two-pronged attack on lymphoma cells and may prove to be an answer for many of our patients."

Preliminary research has shown this combination can prompt tremendous disease regression, and may work better than Rituxan alone. The Wilmot Cancer Center is one of 14 sites in the U.S. offering this investigational combination therapy.

This is one of a series of research studies launched by the newly formed Lymphoma Program at the Wilmot Cancer Center. In the past 18 months, three nationally recognized lymphoma specialists have joined the program and are leading clinical and basic-science research studies.

Leaders of the group, besides Friedberg, include Wilmot Cancer Center Director Richard Fisher, Steven Bernstein, Fay Young, Gordon Phillips II, director of the Blood and Marrow Transplant and Leukemia Program.

For information about this clinical study, or the lymphoma program, call 585-273-4150.

Colorado Researchers Study Massage To Reduce Symptoms

The National Institutes of Health has awarded researchers at the University of Colorado Health Sciences Center a $1.2 million grant to conduct a study to determine if massage therapy reduces the burden of symptoms for cancer patients with advanced disease.

The researchers anticipate the study, the largest

of its kind ever done, will demonstrate that massage therapy decreases pain, improves quality of life and reduces physical and emotional symptom distress among patients with advanced cancer.

During the three-year study, 440 patients nationwide will be enrolled into the randomized clinical trial.

Half of the participants will receive massage therapy, and the other half will receive non-moving touch.

Study participants will agree to six 30-minute therapy sessions over a period of two weeks.

The first participants to enroll will be patients at the University of Colorado Cancer Center Lung Cancer Clinic, Pikes Peak Hospice and Palliative Care and Hospice of St. John.

Initial study enrollment is also supported by a grant from the Mendel Asarch Lung Cancer Family Foundation.

"We have developed a national hospice research network of facilities that will enroll patients later this fall," said Jean Kutner, associate professor of internal medicine at the CU-Health Sciences Center and principal investigator of the study.

"Hospice programs are very interested in the study because they believe massage works," Kutner said. "We anticipate that the study will show that patients who receive the massage therapy will experience a better quality of life during end of life care."

Providers are finding that even in the hospice setting, patients with advanced cancer experience a significant burden of symptoms, including pain, fatigue and decreased appetite, Kutner said.

Proponents of massage and other complementary therapies believe that massage therapy relieves many of these symptoms that are typically managed with medications. With massage, however, patients do not suffer from the side effects that medications can cause.

If the study shows that patients do experience a better quality of life with massage, it could become part of standard patient care. Patients' family members could be trained to give massage therapy outside of the clinical setting.

On the other hand, the study may show that massage does not help patients with advanced cancer.

Kutner said if that is the case, resources that have been allocated for complementary therapies should be redirected.

Published Research:

Longer Infusion More Effective For Pancreatic Cancer

A new study has shown that administering gemcitabine over a longer infusion, at a rate designed to maximize a drug's accumulation in the area affected by cancer, may be more effective than the current standard of treatment for pancreatic cancer.

The study and accompanying editorial, published in the Sept. 15 issue of the Journal of Clinical Oncology, found that this new infusion method—known as fixed dose rate (FDR) infusion—increased the levels of gemcitabine in patients' blood plasma, a surrogate for measuring the amount of gemcitabine in the pancreas, warranting further study to determine the optimal dose and potential clinical benefit of the delivery method.

"Our study is the first to show that FDR infusion yields higher levels of gemcitabine in a patient's blood than standard infusion, potentially paving the way for new and improved treatment regimens," said Margaret Tempero, deputy director of the University of California at San Francisco Comprehensive Cancer Center, and lead author of the study. "These findings indicate that clinical trials examining optimal use of existing chemotherapy drugs are just as critical as trials focused on the development of new drugs."

"If the results of our study are confirmed, they could indicate an exciting new platform for delivering an array of existing chemotherapy drugs, expanding treatment options available to patients," Tempero said.

The study examined 92 patients with locally advanced or metastatic adenocarcinoma of the pancreas, randomly assigning half to receive the standard 30-minute infusion of gemcitabine and the other half to a 150-minute infusion of the same amount of the drug. The study was designed to determine if the longer FDR infusion increased the amount of time before a patient experienced disease progression or became unable to tolerate treatment, a measurement known as time to treatment failure (TTF).

While researchers did not find a significant difference in TTF between patients on the FDR and standard arms of the trial, they did find that average peak levels of gemcitabine triphosphate—the product of gemcitabine that attacks cancer cells—were twice as high among patients on the FDR arm than patients on the standard arm. Overall survival rates increased among those on the FDR arm, compared to those on

the standard arm. The one-year survival rates for patients in the FDR and standard arms were 28.8 percent and 9 percent, respectively. Two-year survival rates were 18.3 percent and 2.2 percent, respectively.

Tempero noted that overall survival rates should be interpreted with caution. When analysis was restricted to patients with metastatic disease—who comprised a majority of study participants—no statistically significant difference in overall survival was found. They also pointed out that 50 percent of patients in the FDR group underwent subsequent chemotherapy, compared to 25 percent of those in the standard group, which could have contributed to patient survival.

Bladder Cancer Survival Rate Rises With Neoadjuvant Chemo

Treating locally advanced bladder cancer with neoadjuvant chemotherapy— chemotherapy before surgery—can offer longer life to patients compared to the standard treatment of surgery alone, according to a study published in the Aug. 28 issue of the New England Journal of Medicine.

In the 11-year study of 307 patients, conducted by the Southwest Oncology Group and led by an investigator at the University of Texas M.D. Anderson Cancer Center, researchers found that patients who received neoadjuvant chemotherapy lived an average of 31 months longer, and that those treated with surgery alone had a 66 percent greater chance of dying from bladder cancer than patients who had the combination therapy.

"This is an important advance, because the study shows a significant and clinically meaningful improvement in survival among patients who received chemotherapy before surgery," said the study's principal investigator, H. Barton Grossman, professor of urology at M. D. Anderson. "Treatment of this disease varies across the country, but we believe neoadjuvant chemotherapy should be used more frequently to treat patients with locally advanced bladder cancer."

Because of its tendency to spread, researchers have investigated a number of therapies to treat transitional cell bladder cancer (the most common form of the disease) which has invaded the bladder muscle and, therefore, is considered locally advanced. Studies to date have found that radiation therapy before surgery did not improve outcome.

With chemotherapy proving beneficial in patients with bladder cancer that had spread to other organs, SWOG began a randomized study in 1987 testing survival in patients who received surgery alone, versus patients treated with a three cycles of a chemotherapy combination known as M-VAC (methotrexate, vinblastine, doxorubicin, and cisplatin) before surgery. The study included 126 institutions around the country.

In all, 154 patients were assigned to receive surgery as primary treatment, and 153 patients received combination therapy. At the end of the study, researchers found that median survival between the two groups was significantly different. Patients treated with surgery lived a median of 41 months, compared to 77 months in patients treated with chemotherapy followed by surgery.

When the investigators looked at death rates from bladder cancer, they concluded that more patients treated with surgery alone died of the disease, and they died at a faster rate—77 patients died of bladder cancer in the surgery arm, compared to 54 in the combination treatment group. Patients treated with surgery alone had a 66 percent greater risk of dying from bladder cancer than patients who received neoadjuvant chemotherapy, according to the research team.

When overall death rates were considered, the results were not as significant, Grossman said. After follow-up of more than eight years in each group, 90 deaths occurred in the combination therapy compared with 100 deaths in the group treated with surgery, meaning that patients who received surgery had a 33 percent greater chance of dying than patients treated with combination therapy, said Grossman.

"These patients are generally older and may die of other causes, but the chance of surviving was higher in the neoadjuvant group," he said.

Patients who did best of all were those who had no cancer left in the bladder at the time of surgery, the researchers concluded. At the time of surgery, significantly more patients (38 percent) had no evidence of cancer remaining in bladder tissue, compared to 15 percent of patients who did not have prior chemotherapy.

"There were significantly more patients in the neoadjuvant group who had no residual disease compared to the surgery group and those are the patients that have much better survival," Grossman said. "The chemotherapy effectively down-staged their cancer. Ten years after treatment, some of those

patients are still alive, so neoadjuvant chemotherapy before surgery provided a cure for them."

The study was supported by grants from the National Cancer Institute.

Almost Half of Faculty on IRBs Have Industry Ties, Study Finds

Medical school faculty members who serve on Institutional Review Boards have extensive research experience and knowledge, yet close to half also serve as consultants to industry, a situation that could lead to potential conflicts of interest, according to a new study in the journal Academic Medicine.

The study provides the first national data on the personal, professional, and research characteristics of faculty members who serve on IRBs in the nation's medical schools and hospitals. IRBs were set up to protect human subjects in clinical research, but many reports have criticized IRBs for failing to adequately protect people participating in research. Some have charged that IRB members were not experienced enough. Others have suggested financial conflicts of interest involving the pharmaceutical industry.

Faculty members, who make up about half of those who serve on IRBs, have extensive research experience and knowledge and often serve as opinion leaders and may guide the board's activities. But the fact that 47 percent of the faculty IRB members who are also researchers served as consultants to industry within three years of the time of the study period (October 2001 to March 2002) may be a reason for concern.

"Our previous research with faculty has shown us that ties to industry can affect scientific behavior, leading to such things as trade secrecy and delays in publishing research," said Eric Campbell, lead author of the study and an assistant professor in medicine at the Institute for Health Policy, Massachusetts General Hospital and Harvard Medical School. "It's possible that similar relationships with companies could affect IRB members' activities and attitudes, although our current study did not directly address this issue."

Almost all faculty who participate on IRBs are involved with research, especially clinical research. This means they tend to have personal research experience and knowledge that may inform their IRB-related activities. But this knowledge could also lead to conflicts of interest of a non-financial nature that should be explored in future research. For example:

—Clinical researchers serving on IRBs may feel pressure not to impede studies important to their individual areas of research, their departments, or to their colleagues, representing a potential non-financial conflict of interest.

—Some faculty IRB members who conduct clinical research may feel pressure to block studies of other investigators when the proposed research might compete with their own studies.

According to Joel Weissman, of the MGH Institute for Health Policy, a co-author of the study, "It is important to note that clinical research experience and relationships with industry can benefit IRBs, since these areas are fundamental considerations when deciding on the appropriateness of a study. However, these benefits must be weighted against the potential risks."

The study, which surveyed 2,989 faculty members from 125 medical schools across the country between October 2001 and March 2002, determined several characteristics of researchers most likely to serve on IRBs.

Among the findings:

—The strongest predictor of IRB participation was race/ethnicity. Under-represented minorities were 3.2 times more likely than white faculty to serve on an IRB. This higher participation may lead to greater attention paid to issues of race/ethnicity in the design and conduct of culturally sensitive clinical trials.

—Of those surveyed who served on IRBs, 73 percent were male, 81 percent were white, 8 percent were Asian, and 11 percent were under-represented minorities.

—Clinical researchers were 1.64 times more likely to serve on an IRB than were faculty who conducted non-clinical research.

—Consulting relationships with industry are common among faculty IRB members.

Finally, the study data indicate that serving on an IRB is not associated with decreased levels of research productivity as measured by publications. The authors indicate several possible reasons: the demands of IRBs are not sufficient enough to impede research activities; IRB service provides members with research ideas and insights; IRB members may be more efficient than non-IRB faculty; or faculty members with high rates of publications are drawn to IRB service.

The study, which was funded by the Burroughs Welcome Fund, the Commonwealth Fund Task Force on Academic Health Centers, The Doris Duke

Charitable Foundation and the Pew Charitable Trusts, was conducted by Campbell, Weissman, Recai Yucel, Nancyanne Causino, and David Blumenthal, all of the Institute for Health Policy, Massachusetts General Hospital and Harvard Medical School; and Brian Clarridge, of the Center for Survey Research at the University of Massachusetts Boston.

Non-Invasive Test May Detect Lung Cancer In Early Stages

Scientists at Duke University Medical Center are developing a non-invasive test that could detect lung cancer in its earliest stages.

The new diagnostic test employs an instrument called MALDI-TOF MS to detect proteins in the blood that signal inflammatory diseases and various cancers. Duke radiologists have identified a specific protein, serum amyloid A, which is elevated in the blood of lung cancer patients but not in the blood of normal patients.

While serum amyloid A has previously been shown to be elevated in cancers and other diseases, the Duke team is the first to use MALDI-TOF MS to identify this protein and others that may be involved in lung cancer, said Edward Patz, professor of radiology and pharmacology/cancer biology at Duke.

Based on the new findings, Patz plans to develop a blood test that will measure serum amyloid A and other, more specific proteins that can detect lung cancer in the blood before a tumor is clinically apparent.

"Our technique is a new paradigm for identifying protein targets in cancer, because we are zeroing in on the disease-causing protein itself rather than searching for a defective gene and then hunting down its relevant proteins," said Patz.

Patz described his methods and results using MALDI-TOF MS (matrix-assisted laser desorption/ ionization time-of-flight mass spectrometry) in two studies published in the September issue of the journal Proteomics.

The Duke studies are proof of principle that MALDI-TOF MS can, in fact, pinpoint and identify proteins in blood that are elevated in cancer and other diseases, said Patz. Moreover, the Duke approach to MALDI-TOF is more sensitive than other diagnostic techniques, he said.

While MALDI-TOF MS is not unique to Duke, Patz has expanded its use in novel ways. Not only does his team record the protein "peaks" in blood samples, he then applies a computer algorithm to each protein that identifies its biologic role in the disease process. The technique requires only a blood sample from the patient. It is more cost efficient and may be more accurate than CT and PET scans, said Patz.

Fish Oil May Help Prevent Weight Loss In Cancer Patients

Fish oil may help to prevent the severe wasting and weight loss, known as cachexia, that characterises some types of advanced cancer, suggests research in Gut, a publication of the British Medical Journal group.

The research team divided 200 patients with pancreatic cancer into two groups: 105 were given a high calorie, high protein supplement; and 95 were given an energy dense, high protein supplement enriched with omega 3 essential fatty acid and vitamin E. Omega 3 essential fatty acids are found in fatty fish, such as herring and salmon.

On average, patients had lost 17% of their body weight and were losing over 3 kilos of weight a month before they started taking the supplements. After eight weeks, there was a direct and significant correspondence between the amount of fish oil enriched supplement patients consumed and the amount of weight and muscle bulk (lean body mass) gained. This was not seen among those patients taking the supplement without the added fish oil. The patients taking the oil enriched supplement also reported a significantly improved quality of life.

IARC Finds Betel Quid, Areca Nut Chewing Causes Cancer

An international working group convened by the Monographs Programme of the International Agency for Research on Cancer, part of the World Health Organization, has found compelling evidence that chewing betel quid without tobacco can cause cancer in humans.

The areca nut, a common component of many chewing preparations, also causes cancer in humans, the group found.

Betel quid generally consists of betel leaf (from the Piper betle vine), areca nut (from the Areca catechu tree), and slaked lime (predominantly calcium hydroxide), to which tobacco is often added. Other ingredients and flavoring agents may be included according to local preferences and practices.

Betel-quid and areca-nut chewing are common in many parts of Asia and among Asian-migrant

communities elsewhere. There is great concern that the habit will spread to populations in North America and Europe not previously exposed to the habit.

The expert group confirmed that betel quid with tobacco causes cancer of the mouth, throat and esophagus. Betel quid without tobacco is also a cancer causing agent. Areca nut, a common component of all betel quid preparations, causes oral submucous fibrosis (a pre-cancerous condition that can progress to malignant oral cancer), allowing the conclusion that areca nut itself is carcinogenic to humans.

This new evaluation of betel quid without tobacco was made possible by recent epidemiological studies from parts of the world where tobacco is not generally added to the betel quid.

Recent studies in India and Pakistan have been able to separate the effects of betel quid use with and without tobacco.

Oral cancers are most common in parts of the world where betel quid is chewed. Of the 390,000 oral and oro-pharyngeal cancers estimated to occur annually in the world, 228,000 (58%) occur in South and South-East Asia.

In some parts of India, oral cancer is the most common cancer. Striking evidence has emerged from Taiwan, where the incidence of oral cancer in men has tripled since the early 1980s, coinciding with a steep rise since the early 1970s, predominantly among men, in the practice of chewing betel quid. Tobacco generally is not added to the betel quid in Taiwan.

In recent years, a variety of mass-produced, pre-packaged areca-nut products have become available in many countries around the world. Aggressive advertising, targeted at all population groups and especially at children, has enhanced the sale and use of these products.

In some parts of India, almost one out of three children and teenagers regularly or occasionally chews these products. Some have viewed such products without tobacco (for example, pan masala) as a safe alternative to betel quid with tobacco. The evidence, however, shows that these products have led to oral disease, even among children, and that use of these products cannot be considered safe. Several Indian states have begun to regulate these products.

The IARC Monographs Programme publishes authoritative, independent evaluations of carcinogenic risks to humans caused by a variety of agents. Further information is available at http://monographs.iarc.fr/

Clinical Trials 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 Study of Active Immunotherapy with CAP-1(6D) and CMV pp65 Peptide-Pulsed, Autologous Dendritic Cells Produced in the AastromReplicell Cell Production System in Patients with Stage IV CEA Expressing Malignancies**.** Duke University Medical, protocol 5910, Lyerly, Kim, phone 919-681-8350.

Phase II

Phase II Study of Bevacizumab and PEG Interferon Alpha-2b (PEG Intron) in Patients with Metastatic, or Unresectable Carcinoid Tumors. M.D. Anderson Cancer, protocol 4772, Yao, James, phone 713-792-2740.

Bevacizumab in Hepatocellular Cancer for Patients with Unresectable Tumor (without Invasion of the Main Portal Vein or Metastatic Disease): A Phase II Study. New York Hospital-Cornell University Medical Center, protocol 5611, Schwartz, Jonathan, phone 212-241-3984.

Phase II Study of Oxaliplatin in Combination with Paclitaxel in Patients with Locally Recurrent or Metastatic Cervical Cancer. New York Hospital-Cornell University Medical Center, protocol 5840, Wadler, Scott, phone 212-746-2844.

Phase II Study of Docetaxel and Capecitabine in Patients with Measurable Metastatic Adenocarcinoma of the Stomach and Gastroesophageal Junction. North Central Cancer Treatment Group, protocol N0242, Jatoi, Aminah, phone 507-284-3077.

Phase III

Randomized Phase III Study of Gemcitabine in Combination with Radiation Therapy Versus Gemcitabine Alone in Patients with Localized, Unresectable Pancreatic Cancer. Eastern Oncology Cooperative Group, protocol E4201, Loehrer, Patrick, phone 317-278-7418.

Phase III Randomized Trial of Cisplatin/ Paclitaxel Versus Cisplatin/Gemcitabine in Recurrent, Persistent or Metastatic Carcinoma of the Cervix. Southwest Oncology Group, protocol S0227, Long, Harry, phone 507-284-4320.