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THE CLINICAL CANCER LETTER

Cancer research news for clinicians

American Association for Cancer Research:

Low-Dose Tamoxifen May Be Effective In Treating Breast Cancer, Study Finds

Administering tamoxifen at lower doses than the current standard dose appears to effectively reduce breast cancer proliferation while causing fewer side effects, according to data published in the Proceedings for the 2003 Annual Meeting of the American Association for Cancer Research.

Unlike standard chemotherapy, estrogen-based agents such as tamoxifen work by saturating the estrogen receptor. Once saturation

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American Surgical Association:

Minimally Invasive Surgery Results In Lower Mortality Rate For Esophageal Removal

Findings from the largest study to date evaluating minimally invasive esophagectomy, or removal of the esophagus to treat esophageal cancer, indicate that the procedure results in lower mortality rates and shorter hospital stays compared with most open procedures.

The results of the study, conducted by James Luketich, associate professor of surgery and chief, division of thoracic surgery, University of Pittsburgh Medical Center and co-director, Lung and Esophageal Cancer Program, University of Pittsburgh Cancer Institute, and Chrish Fernando, also of UPMC, were presented at the annual meeting of the American Surgical Association this month in Washington, DC.

Minimally invasive esophagectomy, or MIE, was evaluated in 221 patients at UPMC from June 1996 through August 2002. Average hospital stays and mortality rates were compared with similar-size studies of open methods including thoracotomy (surgical opening of the chest wall) and laparotomy (surgical opening of the abdomen), or both. The study found that the median hospital stay was seven days for patients who underwent MIE compared with typical hospital stays in excess of 10 days for patients who underwent open procedures. The study also found that mortality occurred in 1.3 percent of the MIE cases compared with typical mortality rates of up to 5 percent or higher as reported for open procedures.

MIE is a video-assisted surgical procedure that utilizes instruments introduced into the body through very small incisions and a laparoscope, or tiny camera. Patients who are candidates for MIE undergo extensive preoperative evaluation involving laparoscopic staging, endoscopic

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Low-Dose Tamoxifen Tested Against Breast Cancer

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occurs, there is no longer any treatment benefit regardless of regimen frequency or dosing, and additional drug may cause an increase in side effects.

"This study demonstrates that tamoxifen doses as low as one milligram per day maintain clinical effect against the treatment of breast cancer," said Andrea Decensi, director of the Division of Cancer Prevention, European Institute of Oncology, Milan, Italy. "Since lower tamoxifen doses may also reduce the risks of potential serious side effects such as endometrial cancer, this study concludes that more drug may not be necessarily better."

The study protocol randomized 120 women with estrogen receptor-positive breast cancer to either one, five or 20 milligrams of tamoxifen daily for four weeks prior to surgery. Results in these women were compared with two non-randomized control groups—one of 34 women with ER-negative breast cancer who were recruited concurrently during the trial, and one of 29 women with ER-positive breast cancer who were recruited after randomization was complete. Changes in Ki-67 (the key identifying marker that measures tumor proliferation and which is associated with tumor shrinkage and prognosis in breast cancer) were measured in cancer tissue before and after tamoxifen treatment.

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Tamoxifen significantly reduced Ki-67 ($p<0.001$) but there was no dose response ($p=0.81$). All three doses reduced Ki-67 levels equally. Although more drug was measured in the tumor at the 20 mg dose, there was no correlation to increased Ki-67 reduction.

"Tamoxifen is the most widely prescribed agent in the world for the prevention and treatment of breast cancer," said Decensi. "Although tamoxifen has been studied since the 1970s, we have yet to determine the optimal biologic dose."

While there may be potential benefits to lower doses of drug in terms of cancer prevention, the study identified other disease markers that were dose-dependent, specifically circulating biomarkers reflecting drug estrogenicity such as insulin-like growth factor-I, cholesterol, triglycerides and antithrombin-III. Lower doses of tamoxifen might therefore reduce its preventative effects in cardiovascular disease and osteoporosis, but also reduce important adverse events such as venous thrombosis. There was also a direct link to the decreased reduction of cholesterol and low dose tamoxifen.

Pain Relievers Protect Against Breast Cancer

Regular use of ibuprofen and aspirin inhibits the formation and growth of breast cancer, according to data published in the Proceedings for the 94th Annual Meeting of the American Association for Cancer Research.

The data, taken from the National Cancer Institute's Women's Health Initiative Observational Study, concluded that weekly doses of non-steroidal anti-inflammatory drugs had a significant effect in reducing the risk of breast cancer.

"These results suggest that even women at high risk for breast cancer may be protected by taking NSAIDs," said Randall Harris, lead investigator of the study, professor of the division of epidemiology and biometrics at the Ohio State University. "However, before usage guidelines for NSAIDs can be implemented, additional studies are needed."

This study found that women taking two or more NSAIDs per week for five to nine years reduced their risk of breast cancer by 21 percent. Extending the use to 10 or more years resulted in an even greater reduction of 28 percent. The probability of developing breast cancer was estimated and adjusted for age and other breast cancer risk factors (e.g. body

mass, estrogen use, family history, and exercise). Researchers observed that ibuprofen was more effective than aspirin in preventing breast cancer (49 percent vs. 21 percent). Regular use of low-dose aspirin (<100 mg) had no effect.

The WHI is an observational study that enrolled 80,741 post-menopausal women between 50 and 79 years of age with no reported history of any cancer, other than non-melanoma skin cancer. Each woman completed a personal interview, which collected information on their individual risk of developing breast cancer and their use of NSAIDs, such as ibuprofen and aspirin. Of those enrolled, 1,392 were later diagnosed with breast cancer.

Based on WHI protocol, each participant provided an annual medical history update. Breast cancer diagnoses were confirmed by WHI physicians using pathology reports. Average follow-up was 43 months. Even after adjusting for demographics and several potential risk factors, the observed effects of long-term use of NSAIDs in reducing breast cancer risk remained stable. The annual incidence of breast cancer in the WHI study (481 cases per 100,000) is similar to the incidence of breast cancer estimated for women over the age of 50, according to the 1998 NCI SEER data (478 per 100,000).

Proteomics Promises Ways To Track Response To Therapy

A new technique may allow physicians to monitor patients' responses to molecularly targeted drugs, according to researchers from the National Cancer Institute and the Food and Drug Administration.

The finding was to have been presented by the NCI-FDA Clinical Proteomics Program at the annual meeting of the American Association for Cancer Research.

In the first study, the researchers successfully identified specific proteins that may be useful in monitoring patients treated for breast or ovarian cancer. Their approach, based on changing levels of active proteins inside tumor cells, could help physicians determine early during treatment whether a particular drug is working effectively for an individual cancer patient.

"The results of our study suggest this approach may help us tailor treatment to individual patients," said Virginia Espina, of NCI, the lead investigator on the study.

Because molecularly targeted drugs are designed to target specific molecules that have gone awry in cancer cells, researchers can predict which of the cell's many complex signaling pathways these drugs are likely to affect. In studies at NCI, researchers are using proteomic technology to monitor the pathways likely to be influenced by the molecularly targeted drugs Gleevec, Herceptin, and Iressa.

To monitor changes in tumor cell proteins, the researchers isolated cancer cells from tumor biopsies and measured the level of various proteins involved in the signaling pathways targeted by the drugs. The scientists measured not only the total amount of each protein, but also how much of the protein was in its active form. These proteins were measured prior to treatment and at selected times after treatment.

The researchers found that prior to treatment, patients with breast cancer who had a poor clinical outcome tended to have more of the active form of a protein known as AKT, which promotes cell survival. Treatment with Herceptin resulted in a change in the relative amount of the active form of AKT, enabling tumor cell death.

"Treatment with Herceptin appears to alter the level of active AKT in tumors," said Lance Liotta, co-director of the Clinical Proteomics Program and the senior NCI investigator on the study. "We may be able to measure the degree of this change in patients who are receiving treatment to determine whether a drug that inhibits this signaling pathway is best for their individual cancer."

In another study, in collaboration with Correlogic Systems Inc., NCI and FDA scientists have improved the NCI/FDA/Correlogic method of ovarian cancer diagnosis. The approach uses Correlogic's artificial intelligence computer programs to analyze the patterns of proteins in the blood and can detect the presence of disease even at early stages.

Researchers used the technique to successfully differentiate between blood samples taken from patients with ovarian cancer and those from unaffected individuals. The researchers discovered patterns of proteins that correctly identify 100 percent of blood samples as being from either unaffected individuals or patients with ovarian cancer. This is an improvement on the previous analysis, which correctly identified 100 percent of the samples from patients with cancer, but only 95 percent of the non-cancer samples. The researchers analyzed the proteins using mass spectroscopy, a technique that sorts proteins

and other molecules based on their weight and electrical charge; they attribute the improvement in specificity primarily to the use of a higher resolution mass spectrometer in the most recent study.

"The increased resolution allows us to distinguish more features within the patterns generated from the serum samples," said Timothy Veenstra, of the Mass Spectrometry Center at NCI-Frederick.

The NCI-FDA team also developed new tools for visualizing and analyzing protein patterns. These tools may allow researchers to determine how far the disease has progressed by matching specific proteomic patterns to a particular stage.

"The new tools improve upon previous methods of identifying discriminatory protein patterns by allowing researchers to visualize the entire set of proteins in a single view, as well as zoom in and out to focus on regions of interest within the data," said Emanuel Petricoin III, co-director of the Clinical Proteomics Program and the senior FDA researcher on the project.

Study Sheds Light On How NSAIDS Prevent Colon Cancer

Building on earlier studies that have shown that non-steroidal anti-inflammatory drugs can reduce the risk of colon cancer in healthy people, researchers at Dana-Farber Cancer Institute have identified a mechanism by which NSAIDs inhibit the development of colon cancer.

Compared with normal cells, colorectal cancer cells have abnormally high levels of an immune system protein, IL-6. David Frank and his Dana-Farber colleagues have discovered that IL-6 triggers malignant growth by activating a protein called STAT1, which transmits signals that prevent the normal scheduled death of cells in the colon.

The findings are published in the Proceedings for the 2003 Annual Meeting of the American Association for Cancer Research.

Frank and his colleagues found that NSAIDs block the IL-6 activation of STAT1, throwing a wrench into the signaling pathway leading to cancer. They showed this by treating colon cancer cells in the laboratory with NSAIDs such as ibuprofen, aspirin and sulindac. They also applied butyrate, a chemical that's produced when the body metabolizes dietary fiber, which also helps protect against colon cancer. Butyrate also blocked IL-6 activity, but through a different signaling pathway.

With these findings in hand, Frank said he and his colleagues are studying ways to block the STAT1 protein in patients who have already developed colorectal cancers.

Hypothyroidism Associated With Reduced Breast Cancer

Women with a common thyroid gland disorder appear to have a reduced chance of developing invasive breast cancer, say researchers at The University of Texas M. D. Anderson Cancer Center.

In a retrospective case-control study of 2,226 females, researchers found that women newly diagnosed with breast cancer were 57 percent less likely to have an under-active thyroid gland, a condition called hypothyroidism, compared to a control group of healthy women.

Also, the breast cancer found in 80 participants who had a history of hypothyroidism was of a less aggressive, indolent variety that was sensitive to estrogen. These women were generally older when first diagnosed with the disease.

"These intriguing findings suggest a possible biological role of thyroid hormone in women with breast cancer that could offer some prognostic or therapeutic value, perhaps suggesting novel preventive strategies," said Massimo Cristofanilli, assistant professor in the Department of Breast Medical Oncology.

The results of the study were published in the Proceedings for the 2003 Annual Meeting of the American Association for Cancer Research.

The influence of thyroid gland disease on breast cancer has been debated for some time, but this is the first study to examine the characteristics of invasive breast cancer in patients with hypothyroidism and compare the incidence of this common condition with a carefully selected matched control group, Cristofanilli said.

"Thyroid hormones and estrogen are both involved in regulating growth in a cell, including cancer cells, so if there is a dysfunction in the ability of a cell to use one hormone, it may potentially affect the capacity of growth regulation of the other," he said.

If results of a prospective trial, now being designed, bear out this conclusion, then it may be possible to design a treatment that specifically and narrowly targets thyroid hormone receptors to help prevent breast cancer.

Statin Drugs May Prevent Breast Cancer, Lab Suggests

Statin drugs used to lower cholesterol may also help prevent development of breast cancer, say researchers who studied the drugs in laboratory cell cultures.

The investigators, from The University of Texas M. D. Anderson Cancer Center, found that a side effect of drugs such as lovastatin and Zocor is to allow body cells to maintain high levels of proteins which stop cancer cells from growing. Their findings were published in the Proceedings for the 2003 Annual Meeting of the American Association for Cancer Research.

"We have found out how a well-known and widely used class of drugs exhibits anti-cancer activities, and that's an exciting finding," says the lead investigator, Ekem Efuet, a postdoctoral researcher working in the lab of Khandan Keyomarsi, associate professor in experimental radiation oncology.

The researchers found that the biological mechanism used by statin drugs to prevent cancer growth may also be the same one used by experimental farnesyl transferase inhibitors now being clinically tested as a cancer treatment.

"We think these experimental agents are targeting the protein degradative pathway, the same way that the statins do," said Keyomarsi. Most of the dose of statin drugs that patients take is converted from its inactive to active form in the liver and used to prevent the synthesis of cholesterol. But the inactive form of the drug that remains in small quantities in the body proves to be a potent cancer fighter, said Efuet.

Several years ago, Keyomarsi lab found that applying lovastatin to cultures of breast cancer cells arrested any further growth, and so they worked to determine what the drug does to produce anti-cancer effects. They found that the pure, unconverted form of the drug (the "closed ring, prodrug" form) stopped cells from activating its proteasome "garbage disposal" to degrade extra P21 and P27 cyclin dependent kinase inhibitors in the cells. These proteins, also known as the brakes of the cell cycle, have been shown to inhibit cancer growth, and so a build-up of P21 and P27 in cells may help prevent cancer formation, say researchers.

On the other hand, the converted ("open ring") form of statin drugs, the form of the drug that lowers cholesterol, was found to have little such anti-cancer activity, proving that the drug works in two different ways, depending on its structure.

The researchers suggest that potent anti-cancer drugs could be developed based on the unconverted form of statins, and they expect to begin testing statin drugs that have already been approved in animal cancer experiments soon.

Leptin Could Be Indicator Of Breast Cancer Risk

Measuring a woman's leptin levels may offer an additional indicator of her risk of developing breast cancer, say researchers at The University of Texas M. D. Anderson Cancer Center.

The small study, published in the Proceedings for the 2003 Annual Meeting of the American Association for Cancer Research, suggests that because a woman's production of leptin may reveal her history of eating dietary fat, reading leptin levels may offer more prognostic information than just measuring body mass index and the amount of fat she currently eats.

Because increased fat is associated with increased bioavailable estrogen and breast cancer risk, "measuring leptin could be an additional marker for assessing breast cancer risk," said the lead author, Richard Hajek, an instructor at M. D. Anderson's Center for Research on Minority Health. "None of these measures are perfect, but the amount of leptin found in a woman's blood stream can indicate her accumulation of fat over the years."

Leptin is produced by fat tissue that signals to the brain when it is time to stop eating. Leptin levels can change according to a pattern of eating. Researchers studied a group of 38 postmenopausal Hispanic women to see how leptin levels fluctuated between women who switched to a high-fiber, low-fat diet and women who switched to high-fiber with no modification in their fat intake. They found that, if body weight and body fat together were not considered, there was a correlation between leptin and the diet. As women ate fewer fat grams, their leptin levels decreased. But many of the patients were overweight, so their leptin levels were high at the beginning of the study.

The volunteers who ate more fiber and less fat reduced their levels of leptin. Leptin levels in these women potentially revealed their lifetime history of eating fat, while examination of their current diet and body fat composition would only offer a "snapshot."

Tumor Cells In Blood May Indicate Aggressive Cancer

If patients with breast cancer have tumor cells circulating in the blood, they may have a more dangerous form of the disease, according to a study by researchers at The University of Texas M. D. Anderson Cancer Center.

The results could lead to more tailored treatment that would spare some patients from the most potent chemotherapy and its toxic side effects.

The study, led by Massimo Cristofanilli, assistant professor of medicine in the Department of Breast Medical Oncology, was published in the Proceedings for the 2003 Annual Meeting of the American Association of Cancer Research, found that women who have tumor cells circulating in the blood have reduced survival compared to those without circulating tumor cells. Until recently, doctors have not been able to reliably isolate circulating tumor cells.

Within the last few years, several methods have been developed to label tumor cells with antibodies that can then be measured precisely, identifying even one tumor cell in a vial of blood, said Cristofanilli. In the current study, the scientists used an automated system developed by Immunicon Corp., Huntington Valley, Pa.

"We know that invasion and metastasis are the most life threatening aspects of cancer," says Cristofanilli. "To metastasize, cancer cells must leave the site of the primary tumor, travel through the blood and proliferate in a new site. If we discovered in a newly diagnosed patient that tumor cells are already in the blood, we would be aware that we are dealing with a more aggressive cancer that may require more aggressive treatment."

In the study, Cristofanilli and his colleagues studied 41 patients who had just been diagnosed with metastatic breast cancer and were about to begin treatment at M. D. Anderson. The scientists found circulating tumor cells in 24 of the 42 patients.

The women who had no circulating tumor cells had a median survival of more than 24 months, while those who had more than three circulating tumor cells survived an average of 13.6 months. Patients with more than 50 cells circulating had a median survival of only 3.8 months. The presence of cancer cells in the blood predicted prognosis more accurately than the site of metastatic disease or the presence of estrogen receptor on the tumor cells, the scientists said.

Brain Gliomas Progress When Gene Function Is Lost

For the first time, researchers are characterizing the molecular processes that turn brain cancer deadly, and their work may result in a diagnostic test that can predict patient survival.

The research, by scientists at The University of Texas M. D. Anderson Cancer Center, demonstrates that degree of loss of a crucial tumor suppressor gene, the AP-2(transcription factor, correlates with progression of different human gliomas.

Researchers found that normal brain tissue, as well as grade II gliomas, maintained expression of AP-2(, whereas 96 percent of grade III glioma, and almost 99 percent of grade IV glioma had lost AP-2(.

"Although previous molecular markers have been identified in malignant gliomas, none have exhibited such a strong correlation with progression, indicating the pivotal role of this gene," says Amy Heimberger, assistant professor in the Department of Neurosurgery.

The findings one day may be clinically important, said Eric McGary, a clinical fellow. If validated through further study, the results can help scientists devise a diagnostic test to check for loss of function of the AP-2(gene, which can help doctors and patients know about treatment options. No such test exists like that now. Heimberger is following the long-term survival of patients within the various grades of gliomas to determine if loss of the AP-2(confers a more serious prognosis.

McGary led the effort to characterize how cancer develops when the AP-2(gene, which normally protects against cancer development, is lost. The researchers found that other tumors such as melanoma become increasingly deadly when the gene is no longer active, and have described its role in breast and prostate cancer as well.

The AP-2(transcription factor controls the expression of many genes, including c-Kit, which regulates cellular proliferation and differentiation, MUC18, an adhesion molecule involved in angiogenesis, and MMP2, which is involved in invasion. When AP-2(is lost, less c-Kit, but more MUC18 and MMP2 are produced, resulting in an increased potential of the cell to grow and divide uncontrollably.

"As such, AP-2(acts as a tumor suppressor gene," says Menashe Bar-Eli, PhD, professor in the

Division of Cancer Medicine and a senior member of the research team.

Looking at tumor samples taken from 279 patients with different kinds of brain cancer, the research team used a tissue array constructed by Dr. Gregory Fuller, associate professor in the Department of Pathology, to look for AP-2(gene expression.

In addition to their findings of different stages of gliomas, they found that 21.5 percent of oligodendrogliomas did not express AP-2(, but this increased to 66 percent in cases of anaplastic oligodendrogliomas. The team also looked at glioblastomas, which are the most common malignant brain tumors in adults and are the most resistant and deadly of all brain cancers to treat. They found that none of the four different glioblastoma cell lines they tested expressed any detectable levels of AP-2(. "The discovery of the ubiquitous loss of AP-2(in high-grade malignant gliomas provides a unique target for new therapies aimed at restoring the function of that gene," says Heimberger. "We are already looking at trying to replace AP-2(function in animal models with gene therapy in order to slow down growth of the tumor," McGary added.

Stem Cell Transplant More Effective than Chemotherapy

Stem cell transplantation is more effective than standard chemotherapy as first-line therapy for patients with multiple myeloma, according to the first evidence-based review of transplant as a treatment option for the disease.

The review was sponsored by the American Society of Blood and Marrow Transplantation and published in the society's journal, Biology of Blood and Marrow Transplantation.

"This information is important for multiple myeloma patients and their physicians as they make treatment decisions and seek reimbursement from health insurers for transplantation," said John Wingard, University of Florida College of Medicine, Gainesville, and chairman of the panel on multiple myeloma.

According to the panel's review:

—Based on the available evidence and expert opinion, stem cell transplant using cells from circulating blood is better than a transplant using stem cells from bone marrow and is the standard of care for the therapy.

—Stem cell transplant is equally effective as therapy for patients who do not respond to treatment with chemotherapy and/or radiation therapy or whose disease recurs after those treatments.

—Stem cell transplant using the patient's own stem cells is currently the standard of care compared to transplant with donor cells, but studies are ongoing to compare and evaluate the roles of the two techniques in the treatment of multiple myeloma.

—A technique in which the stem cells for transplant are harvested from the bone marrow of the patient and treated to remove diseased cells is not an effective treatment for multiple myeloma.

American Surgical Association:
Study Finds Minimally Invasive Esophagectomy Better

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ultrasound and CT scans to assess the extent of the disease.

"Our study demonstrates that minimally invasive esophagectomy offers results as good as, if not better than, open esophageal procedures," said Luketich, who is also co-director of the Mark Ravitch/Leon C. Hirsch Center for Minimally Invasive Surgery at UPMC. "These results are encouraging and demonstrate that MIE can improve patient outcomes without compromising accepted standards of care."

The success of esophagectomy, whether done through standard open approaches or minimally invasively, largely depends on surgical expertise in the procedure and volume of procedures performed annually, Luketich said. He also noted that excellent results using open approaches have been reported from centers that specialize in esophagectomy.

The study included 186 men and 35 women with a median age of 66 years who underwent MIE for esophageal cancer. MIE was successfully completed in 93 percent (205) of the patients. Median stay in the intensive care unit was one day and median hospital stay was seven days. At a mean follow-up of 13.4 months, 90 percent of stage I, 65 percent of stage II and 25 percent of stage III patients had survived their cancer.

These findings have led to the formation of an intergroup trial to assess the results of MIE in a multi-site setting that will include several cancer centers. The multi-site study will be coordinated by the Eastern Cooperative Oncology Group. The primary site for the study will be the University of Pittsburgh Cancer Institute.

FDA Approves HPV Test

The Food and Drug Administration late last month approved expanded use of a laboratory test to detect the presence in women of human papillomavirus.

The test, the HC2 High-Risk HPV DNA Test, manufactured by Digene Corp., of Gaithersburg, Md., can identify 13 of the high-risk types associated with the development of cervical cancer. If left untreated, these changes can eventually lead to cancer in some women.

FDA approved the HPV DNA test in March 2000 for testing women who had abnormal Pap test results to determine whether they needed to be referred for further examination. The new indication allows the test to be used for screening, in conjunction with the Pap test, of women over age 30 for HPV infection. It should be used along with the Pap test, a complete medical history and an evaluation of other risk factors to help physicians determine what kind of follow-up is necessary.

Women who have normal Pap test results and no HPV infection are at very low risk (0.2%) for developing cervical cancer. Women who have an abnormal Pap test and a positive HPV test are at higher risk (6%-7% or greater) of developing cervical cancer if not treated.

Clinical Trials Approved By NCI Last Month Are Listed

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 Pharmacological, and Biological Study of OSI-774 in Combination with FOLFOX 4 (5-FU, Leucovorin, and Oxaliplatin) in Patients with Advanced Colorectal Cancer. Johns Hopkins University, protocol 5869, Hidalgo, Manuel, phone 410-502-3850.

CTLA-4 Blockage with MDX-010 to Induce Graft-Versus-Malignancy Effects Following Allogeneic Hematopoietic Stem Cell Transplantation. University of California, San Diego, protocol 6082, Bashey, Asad, phone 858-657-6790.

Phase I/II

Phase I/II Study of Pre-Irradiation Chemotherapy with Methotrexate Rituximab, and Temozolomide and Post-Irradiation Temozolomide for Primary Central Nervous System Lymphoma. Radiation Therapy Oncology Group, protocol RTOG-0227, Glass, Jon, phone 215-717-3005.

Phase II

Phase II Study of OSI 774 in Combination with Carboplatin and Paclitaxel in Patients with Ovarian or Primary Peritoneal Carcinoma. New York University Medical Center, protocol 5886, Blank, Stephanie, phone 212-263-2527.

Phase II Trial of R115777 in Patients with Metastatic Malignant Melanoma. Cancer and Leukemia Group B, protocol CALGB-500104, Gajewski, Thomas, phone 773-702-4601.

Phase II Study of OSI-774 (Tarceva) and Gemcitabine for Patients with Metastatic Breast Cancer. North Central Cancer Treatment Group, protocol N0234, Perez, Edith, phone 904-953-7283.

Phase II Trial Evaluating Resection Followed by Adjuvant Radiation Therapy for Patients with Desmoplastic Melanoma. North Central Cancer Treatment Group, protocol NO275, Pockaj, Barbara, phone 480-301-8000.

Phase II Study of OSI-774 in Patients with Locally Advanced or Metastatic Papillary Histology Renal Cell Cancer. Southwest Oncology Group, protocol SO317, Gordon, Michael, phone 602-631-4610.

Phase III

Phase III Trial of Treatment of Advanced-Stage Anaplastic Large Cell Lymphoma with Standard APO (Doxorubicin, Prednisone, Vincristine) versus Consolidation with a Regimen Including Vinblastine. Children's Oncology Group, protocol ANHL0131, Kraveka, Jacqueline, phone 843-792-2957.

Phase III Double-Blind, Randomized, Placebo-Controlled Crossover Trial of Black Cohosh (Remifemin) in the Management of Hot Flashes. North Central Cancer Treatment Group, Pockaj, Barbara, protocol 480-301-8000.

Clinical Trial Comparing Preoperative Radiation Therapy and Capecitabine +/- Epoetin Alfa with Preoperative Therapy and Continuous Intravenous Infusion (CVI) of 5-Fluorouracil (5-FU) +/- Epoetin Alfa in the Treatment of Patients with Operable Carcinoma of the Rectum. National Surgical Adjuvant Breast and Bowel Radiation Project, protocol NSABP-R-04, Beart, Robert, phone 323-442-5751.