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THE CLINICAL CANCER LETTER

Cancer research news for clinicians

New Therapeutic Options Enhance Breast Cancer Treatment: ASCO Reports

By Lawrence Prescott

Several novel therapeutic approaches are proving to be of particular value in the treatment of women with breast cancer, according to presentations at the annual meeting of the American Society of Clinical Oncology.

Initial results from the North American Breast Intergroup Trial 0100 point out that women with hormone receptor positive, early-stage breast cancer gain the most benefit if they start taking tamoxifen (Nolvadex, Astra Zeneca) after they have finished chemotherapy, rather than than

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Clinical Trials:

Three Cancer Centers Test Targeted Therapy For Resistant Acute Myelogenous Leukemia

Dana-Farber Cancer Institute has begun a clinical trial of a new drug that kills certain acute myelogenous leukemia cells. The study will test the drug in patients whos AML has resisted other treatments.

The drug, known as PKC412, proved effective in laboratory and animal studies, said Ellen Weisberg, lead author of a study published in the June issue of Cancer Cell.

The trial, being run by Dana-Farber/Partners CancerCare, Memorial Sloan-Kettering Cancer Center, and M.D. Anderson Cancer Center, "will help determine whether PKC412 is effective in AML patients whose bone marrow cells have a particular genetic mutation," Weisberg said. "If it iseffective, PKC412 could take its place alongside Gleevec in a new class of drugs that destroy cells with specific abnormalities while leaving other cells unharmed."

PKC412 zeros in on is a defect in a cell structure called the FLT3 tyrosine kinase receptor. When the receptor is working correctly, it helps ensure that blood-making cells in the bone marrow proliferate and mature properly. When it's defective, because of a genetic mutation, the cells grow out of control and fail to perform their normal function, resulting in AML.

It has been shown that 30 percent of people with AML have a mutation in the gene for FLT3. Weisberg and her colleagues screened dozens of compounds that are known to act against another tyrosine kinase receptor closely related to FLT3.

They found that when AML cells with mutant FLT3 were exposed

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taking the two at the same time, said Kathy Albian, director of Breast Cancer Research and co-director of the Breast Care Center, Loyola University Cardinal Bernardin Cancer Center in Chicago.

"Many women in the U.S. receive tamoxifen and chemotherapy together after surgery, Albian said. "Our results show that it is best to wait until chemotherapy is finished before starting tamoxifen as there is an estimated 18 percent improvement in disease-free survival by delaying tamoxifen until the completion of chemotherapy, rather than giving the two together."

Laboratory evidence has suggested that tamoxifen antagonizes the cytotoxicity of certain chemotherapeutic agents, Albian said.

A phase III trial was carried out to determine if chemotherapy with oral cydophosphamide, doxorubicin, and 5-fluorouracil for 6 cycles plus 5 years of tamoxifen was superior to tamoxifen alone and if CAF followed by tamoxifen was superior to concurrent therapy with CAF plus tamoxifen. A total of 1,477 postpenopausal women with node+, HR+ early-stage breast cancer were randomly assigned to either tamoxifen after chemotherapy (566 pts), tamoxifen and chemotherapy simultaneously (550 patients), or tamoxifen alone (361 pts).

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At eight years follow up, 67 percent of women who received tamoxifen after chemotherapy remained free of breast cancer compared to 62 percent of women who received the two therapies together, and 55 percent of those who received only tamoxifen, Albian said. After accounting for factors that predicted breast cancer recurrence, relative improvement in disease-free survival compared to tamoxifen alone was 44 percent in the patients treated with chemotherapy followed by tamoxifen, versus 23 percent in patients who received the two therapies concurrently, pointing out that women who received tamoxifen after chemotherapy were 18 percent more likely to survive without a cancer recurrence compared to women who received the two therapies at the same time. This translated into a 12 percent absolute benefit over tamoxifen alone. Relative improvement in overall survival compared to tamoxifen alone was 25 percent in the sequentially-treated patients compared to 16 percent in those treated concurrently.

Concurrent chemotamoxifen may result in suboptimal benefit from this or similar chemotherapy programs, potentially cutting efficacy by as much as 50 percent, said Albion.

Nanoparticle Paclitaxel in Metastatic Breast Ca.

A novel albumin-stabilized, cremophor-free nanoparticle formulation of paclitaxel (ABI-007, American Pharmaceutical Partners) has been shown to be well tolerated and very active at both high dose and a dose equivalent to the current FDA approved dose for the cremophor-based formulation of paclitaxel, without the need for steroid pretreatment or granulocyte-colony stimulating factor prophylaxis, said Nuhad Ibrahim, assistant professor of medicine, Department of Breast Medical Oncology, MD Anderson Cancer Center.

"We now have a new formulation of paclitaxel which seems to be more active and less toxic than the present formulation," Ibrahim said. "The fact that ABI-007 is cremophor-free overcomes the limiting effects on paclitaxel availability to tumor cells caused by the cremophor solvent used to solubilize paclitaxel, while improving the safety profile."

These conclusions were reached from two multi-center phase II studies comparing the safety and efficacy of two doses of ABI-007 given as monotherapy in 106 women with histologically-confirmed metastatic breast cancer. The nanoparticle formulation of paclitaxel was administered via a 30-

minute intravenous infusion at 175 mg/m^2 in 43 patients and 300 mg/m^2 in 63 patients, administered once every three weeks without steroid premedication or growth factor support.

Results from study I demonstrate that nanoparticle paclitaxel is well tolerated at high doses of 300 mg/m^2 administered without premedication or growth factor support, with low levels of neuropathy and neutropenia, and no allergic reactions, Ibrahim said. The first-line response rate in the 63 evaluable patients was 88 percent and the overall response rate, defined as complete disappearance or greater than 50 percent tumor mass shrinkage, was 66 percent. In addition, patients who had prior taxane treatment had a 22 percent response rate with high-dose nanoparticle paclitaxel.

When given at the current approved dose of 175 mg/m^2 for cremophor-based paclitaxel formulation, ABI-007 treatment resulted in a 50 percent first-line response rate and a 51 percent overall response rate, Ibrahim said. At that dose, without steroids or growth factor prophylaxis, there were no grade 3 neuropathies, no grade 3 allergic reactions, and only 7 percent of treated patients had grade 4 neutropenia.

Capecitabine in Advanced Breast Cancer

Results of a large, multicenter, phase II trial affirm the unique antitumor activity of capecitabine (Xeloda, Roche) in patients with metastatic breast cancer previously treated with anthracyclines and taxanes, said Pierre Fumoleau, a staff medical oncologist from C.H.R. Gauducheau, Nantes-St. Herblain, France.

"Capecitabine is a very useful drug," said Fumoleau. "Not only has it proved to be safe and effective as a single agent in anthracycline or taxane pre-treated patients but in anthracycline pretreated advanced breast cancer, the addition of capecitabine to docetaxel improved median survival by three months."

"Efficacy was obtained without impairing the patient's quality of life, whether the drug was used as monotherapy or in combination with docetaxel, Fumoleau said. In point of fact, there was improved quaLity of life parameters with regard to both functional and symptom criteria."

A total of 126 women with histologically proven locally advanced or metastatic breast cancer, all of whom had previous treatments with two or three chemotherapeutic regimens including an anthracycline and/or a taxane, received three weekly cycles of oral capecitabine 1250 mg/m^2 twice daily on days 1 to 14, followed by a one-week rest. Anti-tumor efficacy was evaluated every three cycles and progressing patients were discontinued from the study, but included in the final analysis. The primary endpoint was time to disease progression.

Treatment lasted from 1 to 15 cycles, with the median cycles delivered being 6, said Fumoleau. Median treatment duration was 4.1 months. For the 126 patients in the intent-to-treat population, the median time to disease progression was 4.6 months. Best objective response rate was 28 percent, with 4 percent CR and 24 percent PR. In addition, 35 percent of patients had stable disease. The objective response rate at cycle 3 was 19 percent, with 1 percent CR and 18 percent PR, as well as 42 percent of patients having stable disease. So far, one-year survival is 62.3 percent. With the data available at this time, the estimated median overall survival is 15.2 months.

The safety profile of capecitabine was good in this heavily pre-treated population and consistent with earlier pivotal studies, Fumoleau said. Most adverse events occurred within the first 3 cycles, with a maximum occurring in cyle 2. Dose reduction for adverse events was performed in 46 of the 126 patients, with the adverse events leading most frequently to dose reduction being hand-foot syndrome (17.5 percent), neutropenia (7.9 percent) and diarrhea (5.6 percent).

Adding Chemotherapy to Trastuzumab

Adding combination chemotherapy with weekly paclitaxel (Taxol, Bristol-Myers Squibb) and carboplatin (Paraplatin, Bristol-Myers Squibb) following first-line intensified induction trastuzumab (Herceptin, Genentech) single-agent therapy improves patient response and disease control in women with metastatic breast cancer that overexpress the HER2 neu oncogene, said Denise Yardley, director of breast cancer research, Sarah Connor Cancer Center and an associate at Tennessee Oncology, PLLC in Nashville.

"Results of this study show that, in patients with advanced breast cancer, the addition of weekly paclitaxel plus carboplatin to trastuzumab produces improved responses as compared to trastuzumab alone," Yardley said. "In addition, the combination of paclitaxel plus carboplatin is effective in patients who do not respond to first-line trastuzumab."

Initially, 61 women with HER2+ metastatic

breast cancer were enrolled into a phase II trial to evaluate the activity of trastuzumab as a single agent and the benefits of adding weekly combination chemotherapy with paclitaxel and carbo-platin. All patients received a loading dose of 8 mg/kg of trastuzumab followed by 4 mg/kg/week, for 8 weeks. Patients with a minor or better response received another eight weeks of trastuzumab alone, and along with those who had stable disease were then given paclitaxel 70 mg/m^2/week plus carboplatin AUC 2.0/ week in combination with trastuzumab for six weeks, with cycles of eight weeks. Twenty patients failed to respond to trastuzumab and this therapy was discontinued. These women were then treated with weekly combination chemotherapy according to the dosing schedule above.

A total of 58 patients were evaluable for response, Yardley said, with 66 percent demonstrating stable disease or better after first-line trastuzumab and an overall response rate of 22 percent. A 76 percent overall response rate was seen in the 38 patients who responded to trastuzumab and continued to receive weekly trastuzumab along with paclitaxel plus carboplatin. In the 20 patients who failed to respond to trastuzumab therapy and discontinued this drug, administration of weekly paclitaxel plus carboplatin resulted in a 63 percent overall response rate. Median overall survival for the whole group was 29.3 months.

The use of weekly trastuzumab, paclitaxel and carbo-platin was well tolerated by this group of patients, Yardley said. No patients experienced febrile neutropenia and there was no symptomatic cardiac toxicity. In addition, there were no treatment-related deaths.

Five-Year Course of Tamoxifen Remains Standard Treatment In HR+ Breast Cancer

By Lawrence Prescott

Based on the findings from the ATAC (Arimidex and Tamoxifen Alone or in Combination) trial, an American Society of Clinical Oncology panel is of the unanimous opinion that the results of the ATAC trial should be considered preliminary and that a five-year course of tamoxifen remains the standard adjuvant hormonal treatment in women and hormone receptor positive breast cancer, said Eric Winer, director of the Breast Oncology Center, Dana Farber Cancer Institute and associate professor of medicine, Harvard Medical School, at the 38th Annual Meeting of the American Society of Clinical Oncology.

"In an assessment on the use of aromatase inhibitors as adjuvant therapy for women with hormone receptor positive breast cancer, while early results from the ATAC trial indicate an improvement in disease-free survival and a reduction in certain toxicities for anastrozole with or without tamoxifen, there was no survival advantage seen with the combination, said Winer. "Overall, the panel considers the results of the ATAC trial and the supporting data to be very promising but, at this point in time, does not recommend that the combination be used as standard therapy in post-hormonal breast cancer."

The ATAC trial is a randomized, double-blind, multicenter trial with three treatment arms in which postmenopausal women with operable breast cancer were randomized to either anastrozole (Arimidex, Astra Zeneca) 1 mg plus tamoxifen (Nolvadex, Astra Zeneca) 20 mg, tamoxifen 20 mg plus placebo, or anastrozole plus placebo, daily for five years, said Winer. The primary endpoints of the study are recurrence-free survival and tolerability, with secondary endpoints of time to distant recurrence, overall survival, and incident of new primary breast tumors. In total, 9,366 patients from 380 centers in 21 countries were enrolled in the trial between July 1996 and March 2000.

Early results, presented at the 2001 San Antonio Breast Cancer Symposium, indicated an improvement in disease-free survival and a reduction of certain toxicities including fewer reports of endometrial cancer, reduced incidence of thromboembolic events and less vaginal bleeding with anastrozole, compared to tamoxifen, Winer said. In actuality, the absolute differences in disease-free survival between anastrozole and tamoxifen was very small, being 2.1 percent in events, 1.3 percent in distant plus local recurrence, and 0.7 percent in distant recurrence.

When considering these early findings there are a number of concerns to be taken into account, said Winer. The median follow-up of patients is 33 months, with only one-third of patients with followup of more than 3 years. Tamoxifen takes a full five years to see maximal benefit, so the full benefits of treatment with tamoxifen has yet to be realized. Also, despite the encouraging preliminary results, it is conceivable that five years of anastrozole could be inferior to five years of tamoxifen as the ATAC study design does not address the question of how long anastrozole should be continued for optimal therapeutic benefit. Also,

as noted, while the initial differences in disease-free survival are statistically significant, they are very small and there are no reported differences in survival between the two arms.

The short-term side effects are the same or less with anastrozole, except for muscular skeletal disorders and fractures, but there are no data available concerning the toxicity of any of the aromatase inhibitors administered for five years or more. In particular, concern has been raised that the adverse bone effects seen in the ATAC trial could become more common and/or severe with further followup.

Finally, the data from the ATAC trial has not yet been subjected to rigorous peer review and there are no confirmatory trials to date, although they are ongoing. The panel recommended that physicians discuss the available information with patients and, in making a decision, acknowledge that treatment approaches can change over time, said Winer. Individual health care providers and their patients will need to come to their own conclusions, with careful consideration of all the available data.

Study Finds No Link Between Pill And Breast Cancer Risk

Results of the Women's Contraceptive and Reproductive Experiences study of more than 10,000 women show there is no link between taking birth control pills and breast cancer risk.

The study included both white and African American women age 35 to 64, but it did not address the risks and benefits of using oral contraceptives after menopause as hormone replacement therapy.

"Women using oral contraceptives should be reassured from this study, as it confirms that birth control pills do not increase a woman's risk of getting breast cancer," says Kathy Helzlsouer, professor of epidemiology and oncology at the Johns Hopkins Bloomberg School of Public Health.

The investigators also report that several similar studies show oral contraceptives reduce the risks of uterine and ovarian cancers by as much as 40 percent.

The study was published in the June 27 issue of the New England Journal of Medicine.

"New research should focus on developing an oral contraceptive that helps *reduce* the risk of breast cancer, without losing its current cancer preventive effects," said Nancy Davidson, professor of oncology and director of the Breast Cancer Research Program at the Johns Hopkins Kimmel Cancer Center.

The Women's CARE study comes after an analysis of worldwide studies on oral contraceptive use found a slight increase in breast cancer risk among birth control users. In their editorial reviewing the current study, Hopkins experts say the researchers accounted for long-term birth control pill use and a wide range of estrogen and progesterone doses.

While the Hopkins experts conclude that, for most women, the benefits of taking the pill outweigh the risks, they caution, that while rare, oral contraceptives are associated with an increased risk of other conditions, including blood clots, stroke, liver cancer, heart attack in women over 35 who smoke, and cervical cancer in women infected with the human papillomavirus.

Vasectomy Doesn't Increase Prostate Cancer Risk

Contrary to some earlier studies, a new study funded in part by the National Institute of Child Health and Human Development found that men who undergo vasectomies are no more likely to develop prostate cancer than are men who do not.

"About one out of six American men over the age of 35 has had a vasectomy," said Duane Alexander, director of the NICHD. "The results of this study are reassuring since they indicate that these men are no more likely than other men to get prostate cancer."

The study, by Brian Cox and colleagues, was published in the Journal of the American Medical Association.

Although there is no biological explanation why vasectomy might be associated with an increased prostate cancer risk, a few studies conducted in the U.S. in the early 1990s reported a moderately increased risk of prostate cancer among men who underwent vasectomy. Several other studies have found no increased risk of prostate cancer among vasectomized men. However, despite this conflicting evidence, urologists have been concerned enough to increase prostate cancer screening of vasectomized men and to discourage vasectomies in men with a family history of prostate cancer.

This study was conducted in New Zealand, a country considered ideal to examine any possible connection between vasectomy and prostate cancer because, according to the authors, it has both the highest vasectomy prevalence in the world and mandatory reporting of all new cancer cases.

The researchers interviewed over 2,200 men. Almost half of the participants were newly diagnosed prostate cancer patients. The remaining participants were randomly selected from the adult male population and did not have prostate cancer. All participants were between the ages of 40 and 74 and had been married at some time. The men were interviewed by telephone and asked about previous illnesses, vasectomy, smoking and alcohol consumption, prostate specific antigen testing, rectal examination, previous urological symptoms, family history of cancer, and socio-demographic characteristics.

Vasectomized men were no more likely to have prostate cancer than those who had not had a vasectomy. Furthermore, according to the study's authors, "Adjustment for social class, geographic region, religious affiliation, and a family history of prostate cancer, had little effect on the relative risk of prostate cancer from vasectomy."

The study also found that there was no increased risk of prostate cancer among men who had vasectomies 25 or more years before they were interviewed.

Drug Slows Tumor Growth In Metastatic Kidney Cancer

Researchers from the U.S. National Cancer Institute said the molecularly targeted drug bevacizumab slowed tumor growth in patients with metastatic renal cell carcinoma, the most common form of kidney cancer in adults.

The findings from their randomized clinical trial were presented at the American Society for Clinical Oncology meeting in Orlando, Fla.

Tumor growth slowed considerably in trial patients who were given a high dose of bevacizumab. The time it took for the cancer to show measurable growth was two and a half times longer in these patients compared to those who did not receive the drug (approximately five vs. two months). Although the difference was small, it was highly statistically significant. There was also a smaller, but still significant, effect from the lower dose of bevacizumab.

In this phase II trial, 116 patients with advanced cancer and no known effective treatment options were randomly selected to receive placebo, a low dose of the drug (3 mg/kg), or a high dose (10 mg/kg). Because only minimal side effects were associated with the drug, researchers were able to design a double-blind trial, in which neither patients nor physicians knew which treatment was being given.

Like other molecularly targeted drugs, bevacizumab is designed to specifically interfere with a biological process that promotes tumor growth or survival. This drug targets the angiogenic process—the growth of new blood vessels that provide a supply of oxygen and nutrients that are necessary for a growing tumor. Bevacizumab is an antibody that neutralizes the vascular endothelial growth factor (VEGF) protein, one of many proteins secreted by tumor cells to promote the development of a new network of blood vessels. By binding to VEGF, bevacizumab prevents it from triggering blood vessel growth, thereby inhibiting tumor growth.

"The results of this trial are encouraging, demonstrating that anti-angiogenic drugs can inhibit tumor growth in patients," said James Yang, of NCI's Center for Cancer Research, the lead investigator on the study. "This is an important first step toward validating, in patients with cancer, the exciting advances in angiogenesis we have seen in the laboratory. "

More than 20 additional clinical trials are underway to evaluate bevacizumab as a treatment for various types of cancer. The drug is being tested in phase III trials for breast and colorectal cancer. Phase II trials with bevacizumab include those for prostate, breast, colorectal, cervical, ovarian, pancreatic, and lung cancers, as well as for mesothelioma and several types of leukemia.

STI-571 Effects Are Lasting Against GI Stromal Tumors

Most patients with a rare, advanced stomach cancer who receive STI-571 have a lasting response to the drug and experience significant tumor shrinkage, a new study shows.

One year after beginning treatment with STI-571 (Gleevec, imatinib mesylate), over 60% of patients with gastrointestinal stromal tumors (GISTs) had no progression of cancer and could continue taking STI-571. In addition, over 60% of patients had tumors that shrunk by at least half, and another 20% had tumors that shrunk by one-quarter to one-half or stabilized.

"These responses are lasting and are in marked contrast to standard chemotherapy, which has a

response rate of 5%," said Margaret von Mehren, associate member of the Fox Chase Cancer Center in Philadelphia.

In this phase II study, 147 patients received STI-571 (either a 400 or 600 mg dose) daily in pill form. The response rate did not differ substantially between the two dosages. The drug was generally well tolerated, although some patients experienced side effects that included nausea, diarrhea, muscle cramps, and skin rash. About 20% of patients had severe side effects that included low white blood cell counts, tumor hemorrhage, and abdominal pain.

While on the therapy, 14% of patients experienced progression of their cancer. Studies are already underway to learn why a tumor that initially responded to STI-571 has become resistant to the drug, said von Mehren.

Monoclonal Antibody Improves AML Response To Therapy

A new treatment approach for acute myeloid leukemia that combines a monoclonal antibody with chemotherapy helps to improve patients' response to therapy compared to chemotherapy alone, research shows.

Patients in this phase III study had AML that either did not respond to initial treatment or returned following treatment. They were randomly selected to receive chemotherapy alone or in combination with the monoclonal antibody HuM195.

Monoclonal antibodies are genetically engineered proteins designed to target specific antigens on the surface of tumor cells. In this case, HuM195 seeks out and binds to the antigen CD33, which is found on myeloid leukemia cells. This interaction causes the cancer cells to rupture.

"Our results suggest that HuM195 plus chemotherapy should become the standard treatment for patients with AML if their cancer returns or if they don't respond to initial treatment," said Eric Feldman, of the Weill Medical College of Cornell University in New York City. "Further studies will be needed to determine whether HuM195 should be incorporated into the initial treatment of patients with AML."

The combination therapy could be safely given and did not increase the occurrence of chemotherapy-related side effects, the researchers noted. Of the 94 patients who received combination therapy, 27 experienced complete remission, and 13 had partial remission, for an overall response rate of 43%. This compares to an overall response rate of 26 percent in the 97 patients who received only chemotherapy. In this group, 20 patients had complete remission and 5 had partial remission. Patients with partial remission met all the criteria for complete remission but had a lower platelet count.

Mortality rates related to the therapies were similar: 15% for combination therapy vs. 13% for chemotherapy alone. Some patients who received HuM195 experienced mild to moderate flu-like symptoms such as fever and chills.

The sresults are especially significant because about 25% of the patients had a blood disorder, such as myelodysplastic syndrome, before developing AML. These patients are typically resistant to chemotherapy and, as a result are, often are excluded from clinical trials, Feldman said.

Clinical Trials:

Study Finds AML Responds To PKC412 Treatment

(Continued from page 1)

to PKC412, the cells died. When they gave the drug to leukemic laboratory mice with mutant FLT3, all the animals were cured. Further tests confirmed that abnormal FLT3 is indeed the target of PKC412.

Preliminary clinical studies with PKC412 indicate that it does not produce serious side effects. As a result, it could go directly into a phase II trial to test its effectiveness against AML.

Protocols Approved During the Month of June 2002

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 OSI-774 and CPT-11 in Patients with Advanced Solid Tumors. Mayo Clinic, protocol 5351, Pitot, Henry, phone 507-284-4718.

Phase I Study of UCN-01 in Combination with Topotecan in Patients with Solid Tumors. Princess Margaret Hospital, protocol 5518, Hirte, Holger, phone 905-387-9495, ext. 6460.

Phase I Study of the Farnesyl Transferase Inhibitor R115777 in Patients with Myelodysplastic Syndrome. M.D. Anderson Cancer Center, protocol

5625, Kurzrock, Razelle, phone 713-794-1226.

Phase I Study of Oxaliplatin, 5-Fluorouracil, and Leucovorin in Combination with Oral Capecitabine in Patients with Advanced Malignancy. University of Wisconsin, protocol 5904, Mulkerin, Daniel, phone 608-265-8131.

Phase I Brachytherapy Dose Escalating Study Using the Proxima Therapeutics Inc. GliaSite RTS In Patients with Recurrent Malignant Gliomas. NABTT Brain Tumor Consortium, protocol NABTT 2106, Kleinberg, Lawrence, phone 410-614-2597.

Phase I Study of Combined Radiotherapy and Arsenic Trioxide for the Treatment of Newly Diagnosed Malignant Glioma. BrainTumor Consortium, protocol NABTT-2115, Ryu, Samuel, phone 313-916-1027.

Phase I/II

Phase I/II Study of UCN-01 in Combination with Fludarabine in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma. Princess Margaret Hospital, protocol 5538, Crump, Richard Michael, phone 416-946-4567.

Phase I/II Trial of OSI-774 in Patients with Recurrent Malignant Gliomas and Malignant Gliomas Post Radiation Therapy. North American Brain Tumor Consortium, protocol NABTC-01-03, Raizer, Jeffrey, phone 212-639-7330.

Phase II

Phase II, Pharmacokinetic and Biologic Correlative Study of OSI-774, an EGFR Tyrosine Kinase Inhibitor, in Patients with Advanced Renal Cell Carcinoma. Institute for Drug Development, protocol 5410, Tolcher, Anthony, phone 210-616-5914.

Phase II Study of OSI-774 in Advanced Esophageal Cancer. Memorial Sloan-Kettering Cancer Center, protocol 5445, Ilson, David, phone 212-639-8306.

Phase II Trial of ST1571 In Metastatic Breast Cancer. M.D. Anderson Cancer Center, protocol 5580, Cristofanilli, Massimo, phone 713-792-2817.

Phase II Trial of BCNU plus O6-Benzylguanine in the Treatment of Patients With Newly Diagnosed Glioblastoma Multiforme. Duke University Medical Center, protocol 5632, Friedman, Henry, phone 919-684-5301.

Phase II Study of the Farnesyltransferase Inhibitor Zarnestra in Complete Remission Following Induction and/or Consolidation Chemotherapy in Adults with Poor-Risk Acute Myelogenous Leukemia and High-Risk Myelodysplasia. University of Maryland, protocol 5689, Karp, Judith, phone 410-328-9283 (Vonette Yon).

Phase II Trial of Trastuzumab (Herceptin) in Patients With Previously Treated Advanced Urothelial Tract Transitional Cell Carcinoma. Cancer and Leukemia Group B, protocol CALGB-90101, Hussain, Arif, phone 410-328-3911.

Phase II Study of Imatinib Mesylate (Gleevec) in Patients with Refractory Seminoma. Cancer and Leukemia Group B, protocol CALGB-90105, Ryan, Christopher, phone 773-834-1676.

Phase II Study of Reduced Intensity Allogeneic Bone Marrow Transplant for the Treatment of Myelodysplastic Syndromes. Eastern Cooperative Oncology Group, protocol, E1902, Luger, Selina, phone 215-662-7909.

Phase II/III

Phase II/III Study of Immunomodulation after High Dose Myeloablative Therapy with Autologous Stem Cell Rescue for Refractory/Relapsed Hodgkin Disease. Children's Oncology Group, protocol AHOD0121, Chen, Allen, phone 410-614-5055.

Phase III

Randomized Phase III Trial of Cisplatin Versus Cisplatin and Etoposide in Patients with Extensive Stage Small Cell Lung Cancer. Southwest Oncology Group, protocol S0124, Natale, Ronald, phone 310-967-1101.

Phase III Randomized Study of Liposomal Doxorubicin Plus Carboplatin Versus Carboplatin in Platinum-Sensitive Patients with Recurrent Epithelial Ovarian and Peritoneal Carcinoma After Failure of Initial Platinum-Based Chemotherapy. Southwest Oncology Group, protocol S0200, Alberts, David, phone 520-626-7685.

Other

Study to Determine the Effect of Herceptin on Cardiac Function and Cardiac Serum Markers in a Subset of Women Enrolled in NCCTG N9831. North Central Cancer Treatment Group, protocol N0231, Perez, Edith, phone 904-953-7283.

Pilot Trial of Concurrent Docetaxel and a Pox Vector PSA Vaccine Followed by Docetaxel in Metastatic Androgen Independent Prostate Cancer. NCI, Medicine Branch, protocol 5319, Dahut, William, phone 301-435-8183.