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THE CLINICAL CANCER LETTER

Cancer research news for clinicians

San Antonio Breast Cancer Symposium:

Arimidex Reduces Relapse Compared To Tamoxifen, Large Study Reports

New data presented at the San Antonio Breast Cancer Symposium this month report for the first time the effect of Arimidex (anastrozole), as an adjuvant treatment in postmenopausal women with early breast cancer.

After a median of 33.3 months follow-up and a median duration of treatment of 30.7 months, 317 of 3,125 women in the Arimidex group had a relapse of their breast cancer or died, compared with 379 of 3,116 women in the tamoxifen group (p=0.0129). This represents a 17% reduction in

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Clinical Trials:

New Treatment For Malignant Glioma, IL13-PE38, Tested In Early Clinical Trials

A new therapy in the earliest stages of clinical testing can be safely administered to patients with malignant glioma and may provide some potential for treating this incurable brain tumor, according to researchers.

Preliminary phase I/II study data indicate that IL13-PE38 may be effective, safe, and effectively administered by positive-pressure microinfusion. This convection-enhanced delivery, which uses catheters inserted in the brain before or following surgical removal of the tumor, is designed to infuse IL13-PE38 directly to the tumor site and adjacent brain tissue to prevent recurrence of tumor cell growth. The most effective dosage level of IL13-PE38 is being determined in these studies.

The data were presented in three abstracts at the annual meeting of the World Federation of Neuro-Oncology/Society for Neuro-Oncology, held in Washington, DC on Nov. 16.

IL13-PE38 is licensed by NeoPharm Inc. from the U.S. National Cancer Institute and the Food and Drug Administration.

The data represent the first clinical data reported in a scientific forum on IL13-PE38. Presenting the abstracts were Raj Puri, senior investigator and chief, Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapies, FDA; Jon Weingart, assistant professor of neurosurgery and oncology, Department of Neurosurgery, Johns Hopkins University; and Michael Prados, director, Neuro-Oncology Service, Department of Neurosurgical Surgery, University of California San Francisco.

Malignant glioma, which includes glioblastoma multiforme and

(Continued to page 6)

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Disease Reduction Shown With Arimidex In ATAC Trial

(Continued from page 1)

the risk of disease recurrence with Arimidex treatment compared to tamoxifen.

The reduction in the risk of recurrence was 22% in women with confirmed hormone-sensitive tumors with Arimidex treatment compared to tamoxifen (p=0.0054). Arimidex works by reducing circulating estrogen in post-menopausal women. Tamoxifen works by selectively blocking estrogen from stimulating breast cancer cells by binding to the estrogen receptor.

The new data are the first results from the ATAC (Arimidex, Tamoxifen Alone or in Combination) study, the largest breast cancer treatment trial ever conducted. Principal U.S. investigator, Aman Buzdar, of The University of Texas M. D. Anderson Cancer Center, Houston, described the outcome as extremely important for postmenopausal women with early breast cancer.

"Now after 20 years, tamoxifen's established benefits in early breast cancer are being challenged," Buzdar said at the Dec. 10 conference. "Tamoxifen is a very effective drug, but it has side effects, like an increased risk of endometrial cancer, that have to be managed. The goal of research in this area is to improve that profile."

The multi-center, randomized, double-blind study involved 9,366 patients from 380 cancer centers in 21 countries. The trial group consisted of early breast cancer patients who had completed primary surgery and chemotherapy (if given) and were candidates to receive adjuvant hormonal therapy. The trial was designed to determine if Arimidex is equal to, or more effective than, tamoxifen, and whether Arimidex offers additional safety and tolerability benefits.

The study also included a combination treatment arm (tamoxifen + Arimidex) to determine if taking both medications together was better than taking tamoxifen alone. Participating patients were randomized to receive Arimidex (1mg daily), tamoxifen (20mg daily) or a combination of the two treatments for five years or until recurrence of the disease.

Primary trial endpoints were disease-free survival and safety. Secondary end points were time to distant recurrence and survival. There was no additional efficacy benefit seen with the combination arm over tamoxifen alone. In the combination group, 383 of 3125 women had a relapse of their breast cancer or died, compared to 379 of 3116 of women in the tamoxifen group.

Arimidex was associated with significantly fewer reports of endometrial cancer, thromboembolic events (overall incidence and deep vein thromboses) and vaginal bleeding than tamoxifen.

Deep vein thrombosis was reported in 1.7% of the patients taking tamoxifen compared to 1.0% of the Arimidex patients. Endometrial cancer occurred at a rate of 0.5% in tamoxifen patients compared to 0.1% in Arimidex. Vaginal bleeding was reported in 8.1% of tamoxifen patients and 4.5 % of Arimidex patients. Hot flashes and weight gain were also more common among women treated with tamoxifen compared to those taking Arimidex (hot flashes: 39.7% vs 34.3%; weight gain 11.0% vs 9.2%). Women taking Arimidex reported less vaginal discharge and ischaemic cerebrovascular events than women taking tamoxifen (vaginal discharge: 2.8% vs. 11.4%; IC events: 1% vs. 2.1%.)

Women taking tamoxifen reported fewer musculoskeletal disorders or the types of fractures common in this age group, compared to the women taking Arimidex. Fractures (predominantly of the wrist) were reported in 3.7% of tamoxifen patients and 5.8% of Arimidex patients.

The Arimidex/tamoxifen combination treatment group showed no additional tolerability benefits or issues compared with tamoxifen alone.

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The ATAC data will be further analyzed, including sub-protocols designed specifically to investigate the effect of treatment on endometrium, bone and quality of life. Over the next few years, additional follow-up data will be collected to confirm if the observed reduction in relapse rates with Arimidex will impact long-term survival.

Arimidex is FDA approved for first-line treatment of postmenopausal women with hormone receptor positive or unknown locally advanced or metastatic breast cancer and also for treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy.

* * *

Femara Improves Survival: New data from a phase III study demonstrate that Femara may improve survival of postmenopausal women with locally advanced or metastatic breast cancer who are appropriate for hormone therapy, when compared to tamoxifen.

The data, stemming from the largest single study ever to evaluate a hormonal therapy in advanced breast cancer, were announced at the San Antonio Breast Cancer Symposium, San Antonio, Tex.

In commenting on this data, Matthew Ellis, clinical director, Duke Breast Cancer Program, Duke University Medical Center and investigator in the study said, "In the past it was difficult for physicians to decide between letrozole and tamoxifen for initial therapy for their patients with advanced breast cancer because no significant survival benefits had been reported. Now that we have data on letrozole that shows a clear early survival advantage and superior efficacy over tamoxifen, we anticipate a shift to letrozole from tamoxifen in the first-line setting."

The randomized, double-blind study of 907 postmenopausal women (453 on Femara; 454 on tamoxifen) was designed to compare Femara vs. tamoxifen as first-line therapy in women with locally advanced or metastatic breast cancer. Survival rates at one and two years show Femara to have a statistically significant survival advantage compared to tamoxifen.

The data also demonstrated that since initiation of the study approximately five years ago, more women who had begun their therapy on Femara were still alive and free of tumor progression vs. those who took tamoxifen (48 vs. 27, p=0.011). In addition, patients taking Femara had a 78% (p=0.0002) greater chance of responding to treatment than patients treated with tamoxifen. This analysis also confirms that Femara significantly delays progression of disease for a median of 9.4 months, as compared to a median of 6.0 months for tamoxifen (p=0.0001).

As breast cancer advances, it affects a woman's ability to function and perform routine daily activities. Researchers measured the ability of women in the study to complete routine daily activities by using the Karnofsky Performance Score—a standard clinical measurement tool based on a 100 point performance scale (100 being the top performance point) and where a change of 20 points or more is considered clinically relevant.

These results showed that, on average, women taking Femara were able to maintain the level of functioning they experienced when entering the study for a longer period of time than were those women taking tamoxifen. The median time that women taking Femara could more closely maintain the level of functioning they had at study entry (<20 point drop) was more than 4.6 years, while in women taking tamoxifen the median time to experience a significant decrease in performance (>20 point drop) was 3.5 years.

"This new data marks the first time a hormonal therapy has demonstrated a clear, two-year survival advantage over tamoxifen for advanced breast cancer patients," said David Epstein, president, Novartis Oncology.

A related study presented at the conference suggested that Femara may be more effective than tamoxifen in treating postmenopausal women with ER and HER-2 positive breast cancer. The results are based on an analysis of breast tumor samples obtained from a subset of patients in a prospective randomized study comparing the neo-adjuvant use of Femara versus tamoxifen in postmenopausal women. Based on tissue samples taken from a subset of the 337 patients in the clinical study who had confirmed ER+ and ErbB1+ (EGF receptor) and/or ErbB2+ (HER-2/neu receptor) tumors (n=36), had a significantly greater response rate with to Femara than with tamoxifen (Femara 88% vs. tamoxifen 21%, p= 0.0004).

"Data from this study already demonstrates that letrozole is more effective than tamoxifen in treating postmenopausal women with hormone sensitive advanced breast cancer," Ellis said. "These new results suggest letrozole may be effective in treating postmenopausal women with very difficult to treat disease—HER-2 positive breast cancers."

Femara, an aromatase inhibitor, is an oral once-

a-day first-line treatment for postmenopausal women with hormone receptor positive or hormone receptor unknown locally advanced or metastatic breast cancer. The U.S. Food and Drug Administration approved Femara for this indication in January 2001, and it is currently available in more than 75 countries worldwide with first-line approval already gained in more than 50 countries.

* * *

The combination of Xeloda (capecitabine) and Taxotere (docetaxel) significantly improves survival for women with metastatic breast cancer who were previously treated with anthracycline therapy, as compared to Taxotere alone, according to the results from a phase III trial presented in San Antonio.

Post-study analysis also indicates a pharmacoeconomic benefit to the combination over Taxotere alone. The data were the first to have shown that combination therapy has demonstrated superior survival to Taxotere alone in those with metastatic breast cancer.

Sasha Vukelja, of the Tyler Cancer Center, Tyler, Tex., affiliated with US Oncology, presented an update on the phase III trial of Xeloda-Taxotere combination therapy in locally advanced/metastatic breast cancer. Results of this 511-patient study show that the combination of Xeloda and Taxotere:

—Provide a statistically significant survival benefit compared to Taxotere monotherapy (median 14.5 months vs. 11.5 months, log rank $p<0.01$), which amounts to a 22.5 percent reduced risk of death for patients on the combination vs. Taxotere alone (Hazard Ratio=0.777).

—Demonstrated a statistically significant superior tumor response of 32 percent compared to Taxotere monotherapy of 23 percent ($p=0.025$).

—Time to disease progression is significantly longer for patients treated with Xeloda and Taxotere: median 6.1 months vs. 4.2 months with Taxotere alone ($p=0.001$, Hazard Ratio=0.660).

"Xeloda combined with Taxotere is an important treatment improvement for women with metastatic breast cancer," said Vukelja. "The clinical data show significant improvements in survival, tumor response and time to disease progression for the combination compared to Taxotere alone in patients after failure of anthracycline treatment. Based on these data we believe an estimated additional 10 percent of patients with metastatic breast cancer will be alive at the end of 12 months when on Xeloda and Taxotere combination chemotherapy, compared to Taxotere alone."

The study, sponsored by Roche, was conducted in 75 countries including the U.S., Australia and countries in Europe, Asia and Latin America, in patients with metastatic breast cancer previously treated with anthracycline therapy. Patients were randomized into either combination or monotherapy groups.

The combination of Xeloda and Taxotere caused more gastrointestinal side effects and hand-foot syndrome than Taxotere alone. Patients receiving Taxotere alone had a higher incidence of neutropenic fever, myalgia, arthralgia and pyrexia. The spectrum of grade 3/4 toxicities was similar to the profile for all grades. The majority of treatment-related adverse events in both treatment arms were mild to moderate in intensity (83 percent in the combination arm, 86 percent in the monotherapy arm).

The overall incidence of grade 3 treatment-related adverse events was 71percent in the combination arm and 49 percent in the single agent arm; grade 4 treatment-related adverse events were less frequent with the combination regimen (25 percent vs. 31 percent respectively). These were manageable with appropriate medical intervention and by dose interruptions.

Dose reductions decreased the overall incidence of adverse events in subsequent cycles. The number of hospitalizations for treatment-related adverse events was similar in both groups.

The pharmacoeconomic analysis of the Xeloda and Taxotere trial, presented by Joyce O'Shaughnessy, co-director of breast cancer research at Baylor-Sammons Cancer Center, demonstrates a significant cost benefit for the combination therapy compared to Taxotere monotherapy.

According to the data presented:

—Xeloda and Taxotere combination therapy is associated with a cost per life year gained of $4,532.

—Important factors contributing to the cost-effectiveness of Xeloda and Taxotere combination include the superior survival advantage and reduced hospital costs for treatment of adverse events.

—Total cost of Xeloda and Taxotere combination was slightly higher compared Taxotere monotherapy ($21,024 vs. $20,041).

"The additional survival coupled with the cost-benefit of Xeloda and Taxotere combination represents a major advance in the treatment of women with metastatic breast cancer at a minimal incremental cost," said O'Shaughnessy.

In a presentation on post-study follow-up of the participants in the Xeloda and Taxotere Phase III trial, researchers found that patients who initially received Taxotere monotherapy during the trial, then were switched to Xeloda therapy:

—Had a 50 percent reduced risk of death versus other post-study chemotherapy options (p=0.0046).

—When another commonly-used chemotherapy agent, vinorelbine, was given after taxane failure, data showed that there is no decrease in the risk of death and was found to be similar to standard therapy.

A total of 218 patients treated with the Xeloda and Taxotere combination and 198 patients from the Taxotere monotherapy arm received at least one post-study chemotherapy agent and were included in this analysis.

* * *

Researchers investigating the combination of Navelbine (vinorelbine tartrate) Injection, a first-line chemotherapy treatment for advanced non-small cell lung cancer, and the monoclonal antibody therapy Herceptin (trastuzumab), reported an overall response rate of 78 percent in women with HER2 positive metastatic breast cancer, in presenting results of a phase II study at the San Antonio Breast Cancer Symposium.

"The response rate from our multicenter study and a previously reported response rate of 75 percent from an earlier single-site trial are both very encouraging," said Mohammed Jahanzeb, research director of the Boca Raton Comprehensive Cancer Center and professor of biomedical research at Florida Atlantic University, in reference to a single-center investigation at the Dana-Farber Cancer Institute in Boston.

The phase II trial investigated the safety and efficacy of Herceptin and Navelbine as first-line therapy, in metastatic breast cancer, for women with tumors that overexpress HER2 protein.

Forty patients were enrolled in the trial. Weekly intravenous doses of Herceptin and Navelbine were administered over four-week cycles. Thirty-seven patients were evaluated for a response after receiving at least two cycles. A total of four complete responses and 25 partial responses were observed for an overall response rate of 78 percent. Progression of disease occurred in four patients and four remained stable.

After a cumulative total of 313 cycles, significant toxicity, consisting of a grade 4 reduction in neutropenia, was observed in 30% of patients, in 14% of cycles. Grade 3 neutropenia occurred in 50% of patients, in 20% of cycles. One patient was hospitalized with neutropenic fever. There was no severe (grade 3-4) nausea, vomiting, heart disturbance or hair loss reported in the study. Grade 3-4 non-hematologic toxicity consisted of grade 3 fatigue in one patient, grade 4 fatigue in one patient, and grade 3 neurotoxicity in one patient.

These results appear to support previous findings of a single-center investigation at the Dana-Farber Cancer Institute in Boston. In that study, investigators observed responses in 30 of 40 patients administered concurrent weekly doses of Navelbine and Herceptin, for an overall response rate of 75 percent. Grade 3 or 4 neutropenia was observed in 43 percent of patients. Neutropenia was the only reported grade 4 toxicity associated with the treatment. No patients had symptomatic heart failure.

* * *

A phase II study of gemcitabine and Herceptin in previously treated women with metastatic breast cancer resulted in a response rate of about 37 percent, according to a presentation at the San Antonio conference.

Traditionally, either agent alone results in 10-15 percent response rates in women with breast cancer. The study is led by Joyce O'Shaughnessy, of Baylor-Sammons Cancer Center, Dallas.

The study uses gemcitabine 1200 mg/m2, weekly for two weeks with the third week off on a 21-day cycle with weekly trastuzumab 4 mg/kg loading dose, then 2 mg/kg thereafter in Her2+(2 or 3+) metastatic breast cancer patients previously untreated with either Herceptin or gemcitabine.

Fifty-five patients have been entered on the study and 38 were evaluable for toxicity and response. Median age is 53 years and all patients have measurable disease; 20 of 38 pts have ER and/or PR- positive disease, 35 had prior adjuvant chemotherapy; 37 had prior chemotherapy for metastatic disease. Seventeen of 38 patients have metastatic bone disease, 23 liver, 24 lung, and 21 patients with soft tissue disease.

Objective partial responses have occurred in 12 of the 38 (39%) patients and in six of 23 patients (26%) with 3+ HER2 breast cancer. In addition, 16 of the 38 patients have had prolonged stable disease for a median of seven months.

Toxicity: No clinical CHF, 4/38 pts had greater than 15 point decrease in LVEF from baseline with treatment. Grade 3 or 4 toxicities in > 5% pts: asthenia 2/38, fever 4/38, neutropenia 9/38, dyspnea 3/38, chest, abd, back pain 6/38, 3/38 dehydration.

The investigators concluded that gemcitabine plus Herceptin is a safe and effective combination in heavily-pretreated HER2+ breast cancer patients.

* * *

Dose-dense sequential administration of neoadjuvant docetaxel and doxorubicin produced a 24 percent complet pathologic response rate in patients with locally advanced breast cancer, according to a study by researchers at H. Lee Moffitt Cancer Center at University of South Florida.

The preliminary results of the phase II study were presented at the San Antonio symposium.

"This study shows that the sequential combination of doxorubicin and docetaxel given before surgery is a promising approach that can reduce tumor size and subsequently achieve higher rates of breast conservation during surgery," said Susan Minton, lead investigator of the study.

In addition, of those patients known to have axillary lymph node involvement prior to treatment, 30 percent had no evidence of residual disease and 43 percent had three positive lymph nodes at surgery.

The study enrolled 42 women with stage III breast cancer. Thirty-seven completed therapy and had surgery to remove the tumor. All had a tumor or mass greater than 5 cm and were diagnosed with locally advanced breast cancer.

Each drug was given every two weeks rather than every three weeks (dose-dense), and given in sequence rather than together as a combination therapy. This particular timing was chosen to maximize response rate, defined as shrinkage of the tumor.

Patients received 80 mg/m2 of doxorubicin one day every two weeks for a total of three cycles. After a three-week rest, patients received treatment with 100 mg/m2 of docetaxel one day every two weeks for a total of three cycles.

Clinical Trials:

Malignant Glioma Responds To Treatment In Early Studies

(Continued from page 1)

anaplastic astrocytoma tumors, is among the most deadly, invasive and rapidly growing forms of brain cancer. Most people diagnosed with malignant glioma usually live for less than one year after diagnosis, and there are currently very limited treatment options to prevent the rapid recurrence of the cancer once the tumor is surgically removed from the brain.

Based on radiographic scans of the brain, as well as on histopathologic changes of tumor cell death upon microscopic evaluation of brain tumor biopsies prior to surgery and brain tumor tissue removed at surgery, the phase I/II safety and efficacy studies to date indicate that IL13-PE38 may have potential as a treatment for malignant glioma. Additional patients are being enrolled in these studies to validate these early findings.

IL13-PE8 is being developed by NeoPharm under a Cooperative Research and Development Agreement between NeoPharm and the U.S. FDA. Research at FDA has shown that malignant glioma cells, as compared to normal brain cells, express IL13 receptors at a high density. IL13-PE38 is designed to detect and bind to IL13 receptors on the surface of malignant glioma cancer cells. It then selectively delivers a potent cytotoxic agent called PE38 to destroy tumor cells while sparing healthy surrounding cells.

"We're hopeful from the preliminary findings that additional research will demonstrate that patients with malignant glioma can receive a highly targeted, effective treatment at a clinically desirable dose level that kills potent tumor cells without damaging healthy brain tissue," said Puri, who discovered IL13 receptors on tumor cells and IL13-PE38.

Fourteen patients have entered the studies, and enrollment continues. In one study conducted by the New Approaches to Brain Tumor Therapy CNS Consortium, funded by NCI, noticeable response to IL13-PE38 was observed in two of six patients.

One patient, who was treated with IL13-PE38, subsequently underwent surgical removal of the tumor mass. A histopathologic evaluation following surgery found IL13-PE38 effective in destroying approximately 95 percent of the malignant tumor cells.

In a second patient, following IL13-PE38 administration, radiographic scans of the brain revealed a significant reduction in the size of the tumor, and the patient did not require a scheduled, additional, IL13-PE38 infusion.

The complete abstracts are available online at www.soc-neuro-onc.org.

Clinical Trials Approved By NCI In November

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 PS-341 in Combination with Paclitaxel in Metastatic Solid Tumors. Ohio State University Hospital, protocol 1857, Shapiro, Charles, phone 614-293-7560.

Phase I Trial of PS-341 and Carboplatin in Recurrent or Progressive Epithelial Ovarian Cancer or Primary Peritoneal Cancer. Sloan-Kettering Cancer Center, protocol 5326, Aghajanian, Carol, phone 212-639-2552.

Phase I Study of the Toxicities, Biologic and Clinical Effects of Daily 5-Aza-2'Deoxycytidine, for Four Weeks in Patients with Advanced Malignancies. University of Southern California, protocol 5353, Weber, Jeffrey, phone 323-865-3919.

Phase I Trial of 4'-IODO-4'-Deoxydoxorubicin in Primary Amyloidosis. Mayo Clinic, protocol 5718, Dispenzieri, Angela, phone 507-284-2479.

Phase I Clinical and Pharmacological Study of Pyroxamide by Weekly 24-hour Infusion in Patients with Advanced Malignancies. Sloan-Kettering Cancer Center, protocol 5847, Saltz, Leonard, phone 212-639-2501.

Phase I Study of OSI-774 for Solid Tumors in Patients with Hepatic or Renal Dysfunction. Cancer and Leukemia Group B, protocol CALGB-60101, Miller, Antonius, phone 336-716-7975.

Phase I/II

Phase I/II Study of OSI-774 in Combination with Cisplatin in Patients with Recurrent or Metastatic Squamous Cell Cancer of the Head and Neck. OCI-Princess Margaret Hospital, protocol 5380, Siu, Lillian, phone 416-946-2911.

Phase II

Phase II Study of Prostate Specific Antigen-3 with Montanide Vaccination in Patients with Prostate Cancer Recurrent. Univ. of Maryland Cancer Center, protocol 2812, Dawson, Nancy, phone 410-328-2565.

Phase II Clinical, Biological and Pharmacological Study of ZD1839 in Patients with Advanced Colorectal Carcinoma Refractory to 5-Fluorouracil and Irinotecan Chemotherapy. Univ. of Texas Health Science Center, protocol 3753, Hidalgo, Manuel, phone 210-567-4756.

Phase II Study of Gleevec in Ph + Chronic Phase Chronic Myelogenous Leukemia. Children's Oncology Group, protocol AAML0123, Champagne, Martin, phone 514-345-4639.

Phase II Study of Gleevec Mesylate in Children with Refractory or Relapsed Solid Tumors. Children's Oncology Group, protocol AAML0122, Bond, Mason, phone 604-875-3574.

Phase II Trial of Oral Topotecan and Intravenous Carboplatin with G-CSF(Filgrastim) Support in Previously Untreated Patients with Extensive Stage Small Cell Lung Cancer. North Central Cancer Treatment Group, protocol N0027, Jett, James, phone 507-284-3764.

Phase II Study of OSI-774 In Patients With Locally and/or Advanced Metastatic Carcinoma Of the Endometrium. NCI of Canada, protocol NCIC-148, Oza, Amit, phone 416-946-2818.

Phase II Study of OSI-774 Given in Combination with Carboplatin in Patients with Recurrent Epithelial Ovarian Cancer. NCI of Canada, protocol NCIC-149, Hirte, Holger, phone 905-387-9495.

Phase II Trial of Gemcitabine and Irinotecan in Patients with Untreated Extensive Stage Small Cell Lung Cancer. Southwest Oncology Group, protocol S0119, Akerley, Wallace, phone 617-638-7523.

Phase III

Phase II Trial of Chronic roal ZD1839 (Iressa) in both Previously-Untreated and Previously-Treated patients with Selected Stage IIIB and IV Bronchioloalveolar Carcinoma. Southwest Oncology Group, protocol SO126, West, Howard, phone 206-632-1757.

Randomized Phase III Trial of Paclitaxel versus Paclitaxel Plus Bevacizumab (rhuMAB VEGF) as First-Line Therapy for Locally Recurrent or Metastatic Breast Cancer. Eastern Cooperative Oncology Group, protocol E2100, Miller, Kathy, phone 317-274-0920.

Phase III Randomized Study of Patients with High Risk, Hormone-Naive Prostate Cancer: Androgen Blockade with 4 Cycles of Immediate Chemotherapy Versus Androgen Blockade with Delayed Chemotherapy. Radiation Therapy Oncology Group, protocol RTOG-P-0014, Pienta, Kenneth, phone 734-647-3421.

Other

Pilot Study to Evaluate Epidermal Growth Factor Receptor Signaling after Treatment with Oral OSI-774 in Patients with Locally Advanced or Metastatic Breast Cancer. NCI, Medicine Branch, protocol 5403, Swain, Sandra, phone 301-496-0901.

Familiar Factors in the Development of Colon Cancer. Cancer and Leukemia Group B, protocol CALGB-150008, Bertagnolli, Monica, phone 617-732-8910.

Dose Finding Pilot Study of the Safety of Gemtuzumab Ozogamicin Combined with Conventional Chemotherapy for Patients with Relapsed or Refractory Relapsed or Refractory Acute Myeloid Leukemia. Children's Oncology Group, protocol AAML00P2, Sievers, Eric, phone 206-667-5757.

Trials Approved In October

Due to an inaccurate list provided by NCI, **The Clinical Cancer Letter** published identical protocol lists in its October and November issues. Following is the list of trials approved by NCI in October, which should have been published in last month's issue.

Phase I

Phase I Study of a Recombinant Fowl Pox Vaccine rF-CEA (6D)/TRICOM Alone or with GM-CSF in

Patients with Advanced CEA Expressing Adenocarcinomas. Fox Chase Cancer Center, protocol 1133, Von Mehren, Margaret, phone 215-728-2460.

Phase I and Pharmacologic Study of Proteasome Inhibitor PS-341 in Combination with Paclitaxel and Carboplatin in Patients with Advanced Malignancies. Mayo Clinic, protocol 1860, Adjei, Alex, phone 507-284-8964.

Phase I and Pharmacologic Study of 2-Methoxyestradiol in Patients with Advanced Solid Tumors. Mayo Clinic, protocol 3356, Erlichman, Charles, phone 507-284-3514.

Phase I Study of R(+)XK469 in Patients with Advanced Solid Tumors and Lymphoma. Univ. of Chicago, protocol 4570, Ratain, Mark, phone 773-702-4400.

Phase I Study of Epothilone B Analog BMS 247550 in Combination with Carboplatin in Recurrent and/or Refractory Solid Tumors. Moffitt Cancer Center, protocol 5306, Sullivan, Daniel, phone 813-972-4673.

Phase I Trial and Pharmacokinetic Study of BMS-247550, an Epothiline B Analog, in Pediatric Patients with Refractory Solid Tumors. NCI, protocol 5425, Widemann, Brigitte, phone 301-496-7387.

Ex Vivo Selective Depletion of Alloreactive Donor T Lymphocytes Utilizing RFT5-SMPT-dgA, a Specific Anti-Interleukin-2 Receptor Immunotoxin: Reducing Graft-Versus-Host Disease Risk Associated with HLA-matched, Nonmyeloablative, Peripheral Blood Stem Cell Transplantation for Hematologic Malignancies in Older Adults. NIH NHLBI, protocol 5783, Barrett, John, phone 301-496-1434.

Phase I Trial of Interleukin-12 in Combination with Paclitaxel plus Herceptin in Patients with Her2-positive Malignancies. Ohio State Univ. Hospital, protocol 84, Carson, William, phone 614-293-6306.

Phase IB Trial: Treatment of Spontaneous Tumor Metastases with IL-12 DNA. Univ. of Wisconsin, protocol T98-0025, Mahvi, David, phone 608-263-1383.

Phase II

Phase II Study of the Proteasome Inhibitor PS-341 in Patients with Metastatic Breast Cancer. Northwestern University, protocol 1862, Gradishar, William, phone 312-695-4541.

Phase II Trial of Bevacizumab Plus Gemcitabine in Patients with Advance Pancreatic Cancer. University of Chicago, protocol 2675, Kindler, Hedy, phone, 773-702-4400.

Randomized Phase II Study of Bevacizumab in Combination with Docetaxel in Locally Advanced Breast Cancer. Case Western, protocol 2722, Overmoyer, Beth, phone 216-844-3862.

Phase II Trial of Conformal Radiation Therapy for Pediatric Patients with Localized Ependymoma, Chemotherapy Prior to Second Surgery for Incompletely Completely Resected, Differentiated, Supratentorial Ependymoma. Children's Oncology Group, protocol ACNS0121, Merchant, Thomas, phone 901-495-3300.

Phase II Study of Temozolomide in the Treatment of Children with High Grade Glioma. COG, protocol ACNS0126, Cohen, Kenneth, phone 410-614-5055.

Autologous Followed Non-Myeloablative Allogeneic Transplant for Multiple Myeloma. Cancer and Leukemia Group B, protocol CALGB-100001, Anderson, Kenneth, phone 617-632-2144.

Randomized, Phase II ECOG Trial of Two Dose Levels of CCI-779 in Patients with Extensive-Stage Small Cell Lung Cancer Who Have Responding or Stable Disease After Induction Chemotherapy. Eastern Cooperative Oncology Group, protocol E1500, Pandya, Kishan, phone 716-275-9319.

Phase II Study to Evaluate the Effect of Dalteparin and Radiation Therapy on Survival Compared to the RTOG RPA Database and on Thromboembolic Events in Patients with Newly Diagnosed Glioblastoma Multiforme. Eastern Cooperative Oncology Group, protocol E1F01, Robins, Ian, phone 608-263-1416.

Phase II Study of Second-Line SarCNU in Patients with Recurrent/Metastatic Colorectal Cancer. NCI of Canada, protocol NCIC-146, Panasci, Lawrence, phone 514-340-8248.

Phase II Trial of Neoadjuvant/Adjuvant STI-571 for Primary and Recurrent Operable Malignant Gist Expressing the Kit Receptor Tyrosine Kinase (CD117). Radiation Therapy Oncology Group, protocol RTOG S-0132, Eisenberg, Burton, phone 215-28-3096.

Phase II Evaluation of Early Oral Estramustine, Oral Etoposide and Intravenous Paclitaxel in Combination with Hormone Therapy in Patients with High-Risk Metastatic Adenocarcinoma of the Prostate. Southwest Oncology Group, protocol S0032, Smith, David, phone 734-936-8906.

Phase III

Phase III Randomized Trial for Evaluating Second Line Hormonal Therapy (Ketoconazole/Hydrocortisone) vs. Paclitaxel/Estramustine Combination Chemotherapy on Progression Free Survival in Asymptomatic Patients with a Rising PSA after Hormonal Therapy for Prostate Cancer. Eastern Cooperative Oncology Group, protocol E1899, Carducci, Michael, phone 410-614-3977.

Phase III Randomized, Double-Blind, Placebo-Controlled Trial of Gabapentin in the Management of Hot Flashes. North Central Cancer Treatment Group, protocol N00CB, Loprinzi, Charles, phone 507-284-8964.

Detection of Tumor Hypoxia and Vascularity in Patients Undergoing Intraperitoneal Photodynamic Therapy. Univ. of Pennsylvania Cancer Center, protocol 4110, Hahn, Stephen, phone 215-662-7296.

Other

Contemporary Screening for the Detection of Lung Cancer. American College of Radiology Oncologic Imaging Network, ACRIN-6654, Aberle, Denise, phone 310-825-9704.