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THE
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Cancer research news for clinicians

Oral Therapies:

Taking Tykerb With Food Increased Drug Concentration; Paper Urges More Research

A commentary in the Journal of Clinical Oncology urges researchers to explore an intriguing approach to reduce the dose, and therefore the cost, of oral targeted cancer therapies.

The commentary, by Mark Ratain and Ezra Cohen, of the University of Chicago, examines recent pharmacologic research which found that taking the targeted therapy lapatinib (Tykerb) with food significantly increased the concentration of the drug in the body. The commentary suggests that taking lapatinib with food instead of on an empty stomach, as currently indicated,

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Lung Cancer:

Tarceva-Induced Rash Strongly Associated With Longer Survival, Sponsor Finds

The appearance of a rash in cancer patients treated with erlotinib (Tarceva) is strongly associated with longer survival, according to researchers from the drug's developer, OSI Pharmaceuticals Inc.

This is not the first time that rash has been associated with a survival advantage with EGFR inhibitors—a class of drugs which includes erlotinib, cetuximab, panitumumab and others designed to block overproduction of the epidermal growth factor receptor—but it is the most detailed analysis to date.

The study, published in the July 1 issue of Clinical Cancer Research, a journal of the American Association for Cancer Research, reports that for patients taking Tarceva who developed a moderate to severe rash, survival without progression of disease was 245 percent longer than in patients who had a mild rash or none at all.

In the majority of cases, the more severe the rash, the longer a patient's cancer was held in check, researchers found.

This rash, which often looks like acne, can be unpleasant enough for some people to consider discontinuing treatment, but "it is important for physicians and patients to understand that this a positive event because it means there is likely to be a better clinical outcome," said the lead author, Bret Wacker, director of biostatistics at OSI. "Further studies are needed to both identify patients most likely to develop rash and to determine if dose escalation to induce rash can improve efficacy."

Although few patients dropped out of the large phase III clinical trials testing Tarceva in advanced non-small cell lung cancer and pancreatic cancer

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Commentary Urges Research On Dose Reduction With Food

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could cut the needed dose by at least 60 percent, reducing the cost accordingly. The authors stress that formal studies are needed to determine the effectiveness of this approach.

The article was published online July 16.

The commentary focuses on a study presented at the March 2007 meeting of the American Society for Clinical Pharmacology and Therapeutics, which found that lapatinib is more readily absorbed by the body when taken with food, particularly a high-fat meal. As a result, 500 mg of lapatinib taken with food may be as effective as taking the currently approved 1,250 mg without food.

Lapatinib was approved by FDA earlier this year for women with advanced HER2-positive breast cancer. The agency approved the 1,250 mg dose of lapatinib based on a large phase III clinical trial demonstrating its effectiveness and safety at that dose without food. It is taken as five 250 mg tablets on an empty stomach and costs $2,900 per month.

The cost of new targeted cancer therapies—which can be as high as $10,000 per month—has generated substantial discussion and debate.

"The economic implications of this food effect study are particularly remarkable. At the current price of $2,900 per month, this would have a cost savings of 60 percent or $1,740 per month" the commentary states. "As we enter an era of 'targeted' anticancer agents with a monthly cost measured in the thousands of dollars, we should view drug-drug or drug-food interactions as opportunities to lower costs."

The commentary states that rising cancer drug prices are encouraging researchers to explore such pharmacologic approaches to lowering costs. However, the authors urge that neither physicians nor patients consider changing lapatinib dose based on these findings, and that everyone strictly follow the prescribing label directions, which are based on the findings of rigorous clinical tests.

The authors strongly emphasize that a formal pharmacokinetic study of a lower dose of lapatinib with food would need to confirm these findings before any change in dosage could be considered safe and effective.

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Lung Cancer:

Rash May Indicate Stronger Response To Tarceva

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due to the rash, Wacker said he fears those who are taking Tarceva outside of a clinical trial may be likely to stop treatment.

"Some patients are stopping treatment because of the rash, yet those are the ones who are most likely to benefit," Wacker said. "This is a critical problem and rather than permanently discontinue treatment, patients should talk to their doctor about an effective and proactive strategy to manage the rash while continuing Tarceva therapy."

According to the researchers, these rashes can be controlled with mild steroids or antibiotics, and in most cases, they will improve with treatment. They are believed to be due to an inflammatory response as a result of EGFR inhibition in skin tissue, Wacker said.

The analysis looked at two placebo-controlled, double-blind, randomized, phase III clinical trials testing Tarceva in advanced non-small cell lung cancer and pancreatic cancer—studies which led to approval of the agent for treating both cancers. Wacker and his team excluded patients who died in the first month after starting the study because they may not have had time to develop the rash or the rash may have been under-reported in these ill patients.

Of the 673 patients in the lung cancer study, called BR.21, and in the Tarceva-treated group, 81 percent developed a rash, the majority of which was grade 2

(The study graded rashes from 1, relatively mild, to 4, severe).

The researchers found that the presence of any rash correlated with overall and progression-free survival and that these correlations increased with the grade of rash.

Specifically, Tarceva-treated patients who did not develop a rash survived a median of 3.3 months, compared to 7.1 months for those with a grade 1 rash, and 11.1 months for patients with more severe, grade 2 rashes.

They also found, however, that 18 percent of patients treated with a placebo also developed a rash, and that overall survival in these patients was also significantly longer (a median of 8.2 months compared to 4.7 months), compared to placebo patients who didn't develop a rash.

"We don't know why some patients treated with a placebo developed a rash, but it could be due to the strength of their immune system, and that is why they survived longer," Wacker said.

In the second clinical trial (known as PA.3) that tested Tarceva and the chemotherapy drug gemcitabine against a placebo drug and gemcitabine in 521 patients with advanced pancreatic cancer, 71 percent of patients using Tarceva/gemcitabine developed a rash, compared with 30 percent of patients in the placebo group.

This increased rate of rashes in the placebo group makes some sense, Wacker said, because rashes are known to occur with use of gemcitabine chemotherapy. But, unlike the BR.21 study, these pancreatic cancer patients with rashes in the placebo group did not experience an increase in survival compared to placebo group patients without a rash.

In the Tarceva treatment group, only a more severe rash of grade 2 or higher was associated with increased survival.

Patients with a grade 2 rash survived a median of 10.8 months, compared to treated patients with no rash (5.4 months) or a grade 1 rash (5.7 months).

"These different results may be associated with the addition of gemcitabine with Tarceva, or the lower dose of Tarceva in this study, but we just don't know," he said.

Wacker points out that lack of a rash doesn't necessarily mean that patients will not benefit from Tarceva.

"A small percentage of patients who didn't develop a rash still had relatively long survival," he said. "But, still, overall, patients who don't develop a rash don't do as well as those who do."

Breast Cancer:

Breast Cancer Risk Prediction Improved In Atypia Cases

Women with at least three sites of cellular atypia in breast tissue are nearly eight times more likely than average women to develop breast cancer, according to findings of a Mayo Clinic Cancer Center-led study of women with atypical hyperplasia.

The findings are published in the July 1 issue of the Journal of Clinical Oncology.

Several previous studies have shown that atypical hyperplasia (also called atypia) in breast tissue is a major risk factor for breast cancer.

Women who have a breast biopsy and are diagnosed with atypia are considered at high risk. Many are counseled to consider preventive medications such as tamoxifen or other risk-reducing approaches.

However, questions remained from prior research on whether a positive family history further increases risk in women with atypia and for how long the increased risk in women with atypia lasts.

"The most commonly used tool for risk prediction in women with atypia is the Gail model, which may predict inaccurately because our study shows that family history does not change risk significantly in women with atypia," said Amy Degnim, a Mayo Clinic surgeon and study author.

"Our findings indicate that women with atypia have a higher absolute risk for breast cancer than previously estimated," Degnim said. "This risk is 25 percent over 25 years and is much higher in women with multiple areas of atypia and calcification."

The Gail model predicts risk by using age at onset of menses, age at birth of first child, number of previous breast biopsies, presence of atypia, and number of close relatives with breast cancer.

While the Mayo Clinic study found that family history did not further increase risk, age at diagnosis of atypia did affect risk, with younger women (under age 45) more than twice as likely to develop breast cancer compared to women diagnosed with atypia after 55.

The number of areas of atypical hyperplasia was significant as well. With one area of atypia, breast cancer risk was 2.3-fold compared to the general population; this risk more than doubled when two sites were found and increased to nearly eightfold as sites increased to three or more. The group of women with the highest risk had three or more areas of atypia and calcification—with a 10.4-fold risk over the general population.

"With the ability to stratify the risk of breast

cancer in women with atypia, we can have more informed discussions with our patients regarding their personal risk," said Degnim. "This will help us to have individualized discussions regarding how aggressively to pursue risk-reduction treatments."

These findings resulted from reviewing the records of 331 women with atypia identified within the Mayo cohort of 9,376 women who had benign breast biopsies surgically obtained between 1967 and 1991.

More than half (55.9 percent) of the women were over age 55 when diagnosed with atypia, and 42.9 percent had a family history of breast cancer. The majority (68.6 percent) of women showed calcification in the biopsy tissue, and 40 percent had multiple sites of atypical hyperplasia.

Leukemias:

Adding Aresenic To Therapy Improves APL Survival

A study presented at the American Society of Clinical Oncology annual meeting found that the addition of arsenic trioxide to standard therapy significantly increases survival among adult patients with newly diagnosed acute promyelocytic leukemia.

Arsenic trioxide is currently used as second-line treatment for patients who do not respond to the standard therapy.

Standard treatment for APL involves three stages of treatment known as induction, consolidation and maintenance therapy.

In this multi-institutional phase III trial, 257 adults were randomized to receive standard consolidation therapy and 261 adults were randomized to receive two courses of arsenic trioxide in addition to the standard consolidation treatment.

After three years, overall survival was 86 percent in the arsenic trioxide arm versus 77 percent in the standard arm. Event-free survival (survival without experiencing adverse events such as progression of the cancer, death or discontinuation of therapy for any reason) was 77 percent in the arsenic trioxide arm compared with 59 percent in the standard arm.

Cardiac irregularities and blood-related side effects such as low blood counts were not significantly different in the two arms. Other side effects, including infections and headaches, were higher in the arsenic trioxide arm (43 percent versus 28 percent).

"The differences in survival rates and relapse rates are great enough to justify including arsenic trioxide in standard first-line treatment," said Bayard Powell, a professor of hematology and oncology at Wake Forest University Baptist Medical Center, and the study's lead author. "Arsenic trioxide has already shown great benefits as a second-line treatment for APL, a cancer for which patients previously had few good treatment options. This study shows that even more patients will benefit if we give it earlier in the course of treatment."

Dasatinib Active as First-Line Treatment For Chronic Myelogenous Leukemia

Results of a phase II trial conducted by researchers at University of Texas M. D. Anderson Cancer Center in Houston have shown that dasatinib results in high hematologic and chromosomal response rates when used as a first-line treatment for early-stage chronic myelogenous leukemia.

About 4,500 people, mostly adults, are diagnosed with CML in the U.S. each year.

This is the first study to look at dasatinib as a first-line treatment in patients newly diagnosed with the most common stage of CML, called chronic phase. Dasatinib is currently approved as a second-line treatment for CML patients who have developed resistance to imatinib (Gleevec), the standard first-line treatment. Both drugs are targeted therapies that bind to and inhibit BCR-ABL, the mutated protein that causes CML. Imatinib binds to the protein only when it is in its "closed" form, while dasatinib binds to the protein in both its closed and "open" forms.

"These results show that dasatinib elicits a potent chromosomal and hematologic response when used as first-line therapy, and that the side effects are very manageable," said Ehab Atallah, a leukemia fellow at M. D. Anderson and the study's lead author. "Our hypothesis is that patients who have a better early hematologic response may have better progression-free and overall survival, but it is too early to say whether that is the case."

The 31 patients in the study were randomized to receive dasatinib orally, either 50 mg twice a day or 100 mg once a day. The study found no differences between the two dose groups.

After three months, complete hematologic response, defined as normal blood counts and no enlargement of the spleen, occurred in 81 percent of 26 evaluable patients. Complete cytogenetic response, defined as no evidence of the "Philadelphia" chromosome (which encodes the BCR-ABL protein) in the bone marrow, occurred in 73 percent of patients.

After six months, 20 of 21 evaluable patients (95 percent) had complete cytogenetic response. This

compares to previous studies at M. D. Anderson in which 54 percent of patents receiving the lower standard dose of imatinib (400 mg) and 85 percent of patients receiving a higher dose of imatinib (800 mg) had complete cytogenetic response after six months of therapy, though the results of the previous imatinib studies cannot be directly compared to the current dasatinib study.

Researchers will continue to follow the patients in the current trial. In addition, several multi-institutional phase III trials are now enrolling or underway that directly compare dasatinib to imatinib as first-line treatment.

Kidney Cancer:

Bevacizumab Improves PFS In Advanced Kidney Cancer

A large study has shown that adding bevacizumab to interferon-2a as a first-line treatment for advanced kidney cancer nearly doubles progression-free survival. Bevacizumab is currently approved for the treatment of advanced colorectal and non-small cell lung cancers, and is being evaluated in a number of other tumor types.

This is the first randomized phase III trial to confirm its activity in the first-line treatment of kidney cancer.

Historically, there have been very few effective treatments for renal cell carcinoma, the most common type of kidney cancer. In the past 18 months, however, two targeted therapies have proven effective in increasing survival and have received FDA approval—sorafenib (Nexavar) and sunitinib (Sutent).

In this study, 649 patients with advanced kidney cancer who had had surgery to remove their tumors were randomized to receive either bevacizumab or a placebo in addition to interferon.

Adding bevacizumab nearly doubled progression-free survival, from 5.4 months to 10.2 months.

The tumor response rate was 30.6 percent for the bevacizumab group versus 12.4 percent for the placebo group. A trend toward improvement in overall survival was also seen, but longer follow-up is needed to confirm this.

"We're in a very exciting time in kidney cancer research, with a number of new targeted therapies becoming available," said Bernard Escudier, head of the immunotherapy unit at the Gustave Roussy Institute in France and the study's lead author.

The study, called the AVOREN trial, was conducted by a collaborative group of European investigators.

"This study shows the efficacy of yet another agent, with the added benefit of a strong safety profile," Escudier said.

Severe side effects were infrequent and included fatigue (12 percent in the bevacizumab group versus 8 percent in the placebo group), loss of strength (10 percent versus 7 percent) and protein in the urine (7 percent versus 0 percent).

Although the current trial tested bevacizumab in combination with interferon, since the approval of sorafenib and sunitinib, interferon is no longer considered a standard treatment for most patients with renal cell cancer.

Future studies are likely to test bevacizumab as a single agent for first-line treatment of kidney cancer by directly comparing it against sorafenib and sunitinib, as well as evaluating it in combination with those drugs and the experimental drug temsirolimus (Torisel).

Thyroid Cancer:

Axitinib Shows Activity Against Advanced Thyroid Cancer

The first phase II trial to evaluate the experimental drug axitinib in patients with advanced thyroid cancer has shown that the drug has substantial antitumor activity.

The standard treatment for thyroid cancer is surgery and/or radioactive iodine, which cures a large percentage of patients, but there are currently few treatments for patients who do not respond to those therapies.

Axitinib inhibits receptors of vascular endothelial growth factor (VEGF), which plays a role in tumor formation by promoting the growth of blood vessels (angiogenesis).

This single-arm, multicenter trial followed 60 patients who had thyroid cancer that had advanced despite other treatments. Patients received axitinib orally as a pill.

"Axitinib and other VEGF inhibitors represent an exciting new front in the treatment of advanced thyroid cancer," said Ezra Cohen, assistant professor of medicine at the University of Chicago and the study's lead author. "As recently as three years ago we had very little to offer these patients, and now we're seeing response rates at a level we've never seen with chemotherapy."

In this study, 22 percent of patients experienced a partial response, meaning that their tumors shrank (by 31 to 68 percent). This tumor shrinkage lasted from one to 16 months.

In another 50 percent of patients, tumors stopped growing. Blood tests also showed that levels of VEGF

receptors 2 and 3 decreased by 32 percent and 35 percent, respectively, an indication that the drug was binding to its target.

The drug was well tolerated with few side effects. Fatigue was the most common side effect, seen in 43 percent of patients.

The incidence of serious side effects was low and included those commonly seen with this class of drugs: hypertension (7 percent) and protein in the urine (5 percent).

Additional thyroid cancer trials are planned for axitinib, including a phase II trial in patients who have cancer that is no longer responding to the chemotherapy drug doxorubicin, and a phase III placebo-controlled trial in patients with certain subtypes of thyroid cancer.

Ovarian Cancer:

VEGF-Trap Shows Activity Against Ovarian Cancer

Interim analysis of an international, multicenter phase II trial has shown that the targeted therapy VEGF-Trap has activity in patients with the most common type of ovarian cancer that has returned and is resistant to platinum-based chemotherapy drugs.

VEGF-Trap works by blocking angiogenesis, the formation of blood vessels that feed tumors, and is being evaluated in several different types of cancer. This is the first phase II trial to study its effectiveness against epithelial ovarian cancer, which makes up 85 to 90 percent of the approximately 22,000 cases of ovarian cancer diagnosed in the United States each year.

"The results of this study are very promising," said William Tew, an assistant attending physician in the department of medicine at Memorial Sloan-Kettering Cancer Center and the study's lead author. "Most antiangiogenesis drugs have been studied in combination with other chemotherapy agents. There are only a handful of diseases for which these drugs seem to work as a single agent, and ovarian cancer—because of its high dependence on blood vessel growth in order to spread—seems to be one of them. As a result, VEGF-Trap shows potential for patients who have developed resistance to other chemotherapy agents."

Thus far, the trial has randomized 162 patients to receive two different doses of VEGF-Trap: 2 mg/kg or 4 mg/kg of body weight. Patients in the study had two or three prior treatments with chemotherapy for advanced disease and had cancer that was resistant to platinum-based drugs as well as topotecan and/or liposomal doxorubicin, which are the current standard of care. Currently there is no approved treatment option for these patients.

Preliminary results of the first 153 evaluable patients from both dosage groups found that tumors shrank in 8 percent of patients, and tumors stopped growing in 71 percent of patients. Information about which patients are receiving which doses is still blinded, so investigators cannot yet determine if one dose is better than the other. The trial is ongoing and investigators are continuing to recruit up to a total of 200 patients.

Side effects data on all 162 patients included hypertension (40 percent), headaches (37 percent), voice hoarseness (32 percent) and protein in the urine (14 percent). A small number of patients (1 percent) experienced bowel perforation, a potentially fatal side effect that has been observed with a higher incidence in other studies of antiangiogenesis drugs for ovarian cancer.

Lung Cancer:

No Benefit To Shark Cartilage As Treatment, Large Trial Finds

In the first scientific study of its kind, shark cartilage extract, AE-941 or Neovastat, has shown no benefit as a therapeutic agent when combined with chemotherapy and radiation for patients with advanced non-small cell lung cancer, according to researchers at The University of Texas M. D. Anderson Cancer Center.

Charles Lu, associate professor in M. D. Anderson's Department of Thoracic/Head and Neck Medical Oncology, presented the study at the annual meeting of the American Society of Clinical Oncology.

The absence of blood vessels in cartilage as well as preclinical studies analyzing cartilage extracts have supported the hypothesis that cartilage contains inhibitors of angiogenesis. Also, shark cartilage has long intrigued the public due to the belief that the incidence of cancer in this cartilaginous fish is very rare. Early Phase I and II studies in lung and renal cancers suggested some benefit to patients when AE-941 was given at higher doses, says Lu.

"This is the first large phase III randomized trial of shark cartilage as a cancer agent. A unique and important aspect about this shark cartilage study was that this product, Neovastat, was never sold over-the-counter, unlike other shark cartilage compounds previously studied. The company, Aeterna Zentaris, developed the compound as a pharmaceutical as opposed to a compound sold for profit that is available over the Internet, for example," said Lu, the study's national

principal investigator.

The international phase III study enrolled 384 newly-diagnosed untreated Stage III non-small cell lung cancer patients at 53 sites in the United Sates and in Canada from June 2000 to February 2006. M. D. Anderson enrolled 60 patients in the trial.

The study was initiated at the request of, and was supported by, the National Cancer Institute who sought proposals from pharmaceutical companies regarding their shark cartilage agents.

All study participants received the standard treatment of induction chemotherapy and chemo-radiation. Patients were randomized to receive either shark cartilage or placebo, both in the form of a liquid. Patients drank four ounces of the extract twice daily, and continued on the shark cartilage/placebo as maintenance after completing standard therapy.

Researchers say that the study did not meet its primary endpoint: survival. With a median follow-up of 3.7 years, researchers did not find a statistical difference in survival between patients who received the shark cartilage, 14.4 months, and those who received the placebo, 15.6 months.

"Clearly, these results demonstrate that AE-941 is not an effective therapeutic agent for lung cancer," said Lu. "So, too, these findings have to cast major skepticism on shark cartilage products that are being sold for profit and have no data to support their efficacy as cancer-fighting agent."

Patients who are currently taking shark cartilage should be very cautious in accepting that the therapy will be beneficial, Lu said. "We have absolutely no data showing improvements in survival, tumor shrinkage and/or clinical benefits to patients," Lu said. "Now when patients ask their oncologists about shark cartilage, physicians can point to this large NCI-sponsored phase III trial and tell patients that, at this point, the only studies that have been done with cartilage-derived products have been negative."

Aeterna Zentaris, of Quebec, Canada, said earlier this year that it stopped clinical development the compound. Both the NCI and Aeterna Zentaris supported the study.

Cervical Cancer Prevention:

HPV Vaccine Cervarix Active In 100% Of Women In Study

New phase III data show that at 18 months after the first of a three-dose regimen, 100 percent of women up to age 55 vaccinated with the GlaxoSmithKline cervical cancer candidate vaccine Cervarix had antibodies present against the two most common cancer-causing human papillomavirus types, 16 and 18.

These data indicate that the vaccine, formulated with a proprietary adjuvant system called AS04, is highly immunogenic and generally well-tolerated, with antibody levels at least 10 times greater than those produced by natural infection. These new extended follow-up data were presented at the American Society of Clinical Oncology annual meeting.

"Previous natural infection with these cancer-causing human papillomavirus types may not confer lifelong protection," said Tino Schwarz, Stiftung Juliusspital, Wuerzburg, Germany, the lead study investigator. "Thus, women of all ages may be at risk for future infection. In fact, the older a woman is when infected, the more likely that the infection will become persistent, which may lead to the development of precancerous lesions. These GSK cervical cancer vaccine study results suggest that many women could potentially benefit from vaccination against cervical cancer."

Furthermore, the study shows that antibody levels in women ages 26 to 55 against cancer-causing virus types 16 and 18 were in the same range as observed in a separate study. That study demonstrated that the GSK cervical cancer vaccine provided 100 percent sustained protection against precancerous lesions caused by these virus types for up to 5.5 years in women ages 15 to 25.

Healthy women from Germany and Poland ages 15 to 55 who received three doses of the GSK cervical cancer candidate vaccine at 0, 1 and 6 months in this Phase III clinical study were invited to participate in an extension to the initial study, previously evaluated at 12 months. The 517 women who participated in this follow-up study were age-stratified: 15-25 [n=169], 26-35 [n=83], 36-45 [n=89] and 46-55 [n=176] years old. Immunogenicity and safety were assessed at 18 months after the first dose of a three-dose vaccination regimen.

GSK submitted a Biologics License Application to FDA for Cervarix in March 2007, for the prevention of cervical cancer and precancerous lesions associated with the most common cancer-causing HPV types. In May, Cervarix was granted a license by the Therapeutic Goods Administration of Australia for the prevention of cervical cancer and precancerous lesions caused by HPV types 16 and 18 for use in females ages 10-45 years. GSK has also submitted marketing authorization applications to the European Medicines Agency, Canada and numerous countries in Asia and Latin America.

NCI Cooperative Group, Cancer Center Trials Listed

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

Phase I

Phase I and Pharmacokinetic Study of Vorinostat for Solid Tumors and Lymphomas in Patients with Varying Degrees of Hepatic Dysfunction. University of Pittsburgh, protocol 8057, Ramalingam, Suresh, phone 412-648-6619.

Phase II

Phase II Study of VEGF Trap in Patients with MDS. City of Hope National Medical Center, protocol 7518, Zain, Jasmine, phone 626-256-4673, ext. 62405.

Phase II Study of GW786034 (Pazopanib) in Patients with Recurrent and/or Metastatic Invasive Breast Carcinoma. University Health Network-Princess Margaret Hospital, protocol 7638, Pritchard, Kathleen, phone 416-980-4616.

Randomized Controlled Phase II Evaluation of Megestrol (Megace) in Different Dose and Sequence in the Treatment of Endometrial Intraepithelial Neoplasia from a Referred Cohort of Atypical Endometrial Hyperplasia or EIN. Gynecologic Oncology Group, protocol GOG 0224, Method, Michael, phone 574-237-1328.

Phase II Evaluation of Cetuximab in the Treatment of Persistent or Recurrent Squamous or Non-Squamous Cell Carcinoma of the Cervix. Gynecologic Oncology Group, protocol GOG-0227E, Santin, Alessandro, phone 501-296-1099.

Phase III

Response and Biology-Based Therapy for Intermediate-Risk Neuroblastoma. Children's Oncology Group, protocol ANBL0531, Twist, Clare, phone 650-723-5535.

Phase III Randomized Trial of Small (</= 2 cm) Peripheral Non-small Cell Lung Cancer. Cancer and Leukemia Group B, Altorki, protocol CALGB-140503, Nasser, phone 212-746-5156.

Phase III Study of Active Surveillance Therapy Against Radical Treatment in Patients Diagnosed with Favorable Risk Prostate Cancer. National Cancer Institute of Canada Clinical Trials Group, protocol NCIC CTG PR.11, Klotz, Laurence, phone 416-480-4673.

Pharmacokinetic, Pharmacodynamic and Pharmacogenetic Study of Nab-Paclitaxel(Nanoparticle Albumin Bound-Paclitaxel) in Patients with Advanced Solid Tumors. Eastern Cooperative Oncology Group, protocol E1Y06, Mani, Sridhar 718-904-2529.

FDA Approves Molecular Test For Breast Cancer Detection

FDA approved the first molecular-based laboratory test for detecting whether breast cancer has spread to nearby lymph nodes.

The GeneSearch BLN Assay detects molecules that are abundant in breast tissue but scarce in a normal lymph node. The test is manufactured by Veridex, a Johnson & Johnson company, of Warren, N.J.

During a lumpectomy or mastectomy to remove a breast tumor, surgeons commonly remove the sentinel node for examination under a microscope. Sometimes the sentinel node is examined immediately and if tumor cells are found, additional lymph nodes are removed. A more extensive microscopic examination, requiring one to two days for results, is almost always performed. If tumor cells are only found with the later microscopic examination, the patient may require a second surgery to remove the remaining lymph nodes.

"The GeneSearch BLN Assay offers a new approach to sentinel node testing," said Daniel Schultz, director of the FDA's Center for Devices and Radiological Health. "Results of this rapid test are available while patients are on the operating table, providing a way for some women to avoid a second operation."

In a clinical trial, the GeneSearch BLN Assay showed strong agreement with results from extensive microscopic examination of the lymph nodes of 416 patients. The test accurately predicted that breast cancer had spread nearly 88 percent of the time in women with metastasis. Patients without metastasis were identified accurately 94 percent of the time.

Most of the women were also studied to compare the BLN Assay with immediate microscopic examination during surgery. The test gave fewer false negative results, but slightly more false positive results. A false negative test result, when the cancer has actually spread, may delay the needed removal of additional lymph nodes. A false positive test, indicating metastasis when there is none, may result in a more extensive surgery and puts the women at risk of unnecessary lymphedema (swelling due to fluid build-up following lymph node removal) and other side effects.