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THE
# CLINICAL CANCER LETTER

*Cancer research news for clinicians*



*Multiple Myeloma:*

## ASCO Updates Clinical Recommendations On Use Of Bisphosphonates In Myeloma

The American Society of Clinical Oncology has updated its recommendations on the use of bisphosphonates, medications that help strengthen the bone, in people with multiple myeloma. The new guideline will be published in the June 10 issue of the Journal of Clinical Oncology.

The key recommendations in the guideline address therapy duration, dosage and monitoring; osteonecrosis of the jaw; and previous recommendations for solitary plasmacytoma, indolent myeloma, smoldering myeloma,

(Continued to page 2)

*Acute Leukemias:*

## Blood Test Could Predict Relapse, Survival For Children, Young Adults With Leukemia

A simple blood test could predict relapse or survival for children and young adults with acute leukemias, researchers from the Children's Cancer Hospital at The University of Texas M. D. Anderson Cancer Center reported at the American Society of Pediatric Hematology Oncology's annual meeting May 5.

A review of young leukemia patients over the past decade has shown that the absolute lymphocyte count (ALC), a measure of normal immune cells found on every complete blood count report, is a powerful predictor of survival for young patients with leukemia.

According to the American Cancer Society, the average rate of survival for pediatric patients with acute myelogenous leukemia (AML) is close to 50 percent. However, researchers have found that using the ALC count on day 15 after initial chemotherapy treatment can significantly predict which patients are likely to relapse and those who will not.

This prediction may help physicians decide how aggressively to treat a leukemia patient. In addition, it may direct researchers in developing therapies to increase a patient's ability to battle the leukemia cells.

"Possibly by tweaking the immune system through chemotherapy, immune modulators or oral supplements, we could help a patient's body better fight leukemia," said Guillermo De Angulo, researcher and fellow at the Children's Cancer Hospital at M. D. Anderson. "This ALC test could also help us identify patients who would benefit from less chemotherapy."

The report studied 171 patients with either AML or acute lymphocytic leukemia (ALL), 21 years or younger, who had begun treatment at M. D.

(Continued to page 4)



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## ASCO Offers Guidelines On Bisphosphonate Use

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monoclonal gammopathy and biochemical markers.

Patients who receive bisphosphonates when being treated for multiple myeloma may experience less bone pain, fewer fractures and slower loss of bone mass. Risks of bisphosphonate use include reduced kidney function, acute kidney failure and osteonecrosis of the jaw.

FDA has approved two intravenous bisphosphonates for treating bone loss from multiple myeloma: pamidronate (Aredia) and zoledronic acid (Zometa).

The guideline recommends that bisphosphonates be given to patients monthly for two years. At two years, the physician should consider stopping the use of bisphosphonates if the patient has responded to therapy. Physicians should re-start bisphosphonate therapy if a patient's myeloma returns and new bone problems develop.

The guideline recommends that people with multiple myeloma who experience bone loss or fracture of the spine from osteopenia receive either 90 mg of pamidronate over two hours or 4 mg of zoledronic acid over at least 15 minutes, every three to four weeks.

The guideline recommends monitoring multiple myeloma patients receiving bisphosphonate therapy every three to six months for albuminuria—high levels of the protein albumin in the urine might indicate damage to the kidneys.

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According to FDA-approved labels of pamidronate and zoledronic acid, the physician also should monitor levels of creatinine, a chemical in the body used to measure kidney function, before providing a dose of either drug.

"Physicians should stop administering pamidronate and zoledronic acid to patients who develop kidney problems while on either bisphosphonate," said Kenneth Anderson, co-lead author of the guideline and director of the Jerome Lipper Multiple Myeloma Center at the Dana-Farber Cancer Institute in Boston. "Treatment may be resumed once the exact kidney problem is identified and resolved."

For multiple myeloma patients with existing kidney problems and extensive bone disease, the guideline does not recommend use of zoledronic acid. For these patients, the guideline recommends a longer infusion of four to six hours of pamidronate, instead of a two-hour infusion.

The guideline also recommends lowering the dose of pamidronate in multiple myeloma patients with pre-existing mild to moderate kidney disease. The manufacturer of Zometa previously recommended lowering the treatment dose for these patients as well.

The guideline includes new recommendations for patients with osteonecrosis of the jaw, or bone loss or deterioration of the jaw that occurs in some patients using bisphosphonates. Symptoms include infection of the jaw, pain, swelling, loose teeth and exposed bone.

"The guideline recommends that all multiple myeloma patients receive a comprehensive dental examination and appropriate preventive dentistry prior to starting bisphosphonate therapy. All oral infections and areas in the mouth at high risk for infection should be treated," said Robert Kyle, co-lead author of the guideline and a hematologist at the Mayo Clinic in Rochester, Minn. "Patients should maintain excellent oral hygiene and avoid invasive dental procedures, if possible, while receiving bisphosphonate therapy."

The guideline update does not recommend use of bisphosphonates for myeloma patients with the following conditions: one bone tumor (solitary plasmacytoma); a slower growing form of myeloma (smoldering or indolent myeloma); or conditions of abnormal plasma cells that are not myeloma but may eventually develop into myeloma (monoclonal gammopathy of undetermined significance).

Also, the guideline does not suggest use of the biochemical markers to monitor bisphosphonate treatment for routine care of multiple myeloma patients.

## Low Dose Therapy Improves Survival Of Multiple Myeloma, ECOG Finds; Update At ASCO

Preliminary results from a large, randomized clinical trial for patients with newly diagnosed multiple myeloma, a cancer typically found in bone marrow, has shown that use of a low dose of the steroid dexamethasone (Decadron), in combination with lenalidomide (Revlimid) is associated with improved survival when compared to a treatment regimen with lenalidomide and a higher, standard dose of dexamethasone.

The clinical trial was sponsored by NCI and conducted by a network of researchers led by the Eastern Cooperative Oncology Group.

The data monitoring committee overseeing the trial (known as E4A03) recommended that the survival results from a recent interim analysis be made public because of early differences being seen in overall survival rates. Researchers found that patients in the study who received low-dose dexamethasone and lenalidomide had a one-year survival of 96 percent compared to 86 percent for patients treated with the standard-dose of dexamethasone and lenalidomide. Also, there were fewer side effects associated with the low-dose dexamethasone and lenalidomide.

Detailed results from this trial will be presented at the American Society of Clinical Oncology annual meeting in Chicago.

"These results have major implications for myeloma therapy," noted study chair Vincent Rajkumar, Mayo Clinic, Rochester, Minn. "The results of this study, particularly lenalidomide plus low-dose dexamethasone, are very positive and in my opinion represent a real step forward in the treatment of this disease."

A total of 445 patients with newly diagnosed multiple myeloma, who had not previously received chemotherapy, were enrolled in this study between 2004 and 2006. Patients were randomized to one of two treatment arms. One patient group received lenalidomide and dexamethasone given at standard doses. The second group received standard-dose lenalidomide and low-dose dexamethasone.

The primary objective was to determine if the low-dose arm would have similar response rates and lower toxicity than the standard-dose arm.

"Randomized trials are the gold standard for evaluation of the effectiveness of new treatments," said NCI Director John Niederhuber. "These results also emphasize once again the importance of NCI's rigorous program of oversight, which brings highly qualified clinician scientists to serve as members of data safety and monitoring committees."

Lenalidomide, a derivative of thalidomide, was approved by the U.S. Food and Drug Administration in 2006 to be used in combination with dexamethasone for the treatment of multiple myeloma in patients who received at least one prior therapy for their disease. Dexamethasone is a steroid that acts as an anti-inflammatory and as an immunosuppressant and has numerous uses in medical practice.

"ECOG has a long history in developing new treatments for multiple myeloma", according to Robert Comis, ECOG group chairman. "The application of this effective and less toxic approach will benefit many patients with this disease."

Celgene, Inc., Summit, N.J., which manufactures lenalidomide, provided lenalidomide under a Clinical Trials Agreement with NCI for the clinical development of lenalidomide.

Based on the ECOG findings and early analysis of its own data the Southwest Oncology Group, the largest of the NIH sponsored multi-center cooperative groups, has brought its trial of high dose dexamethasone versus Revlimid plus high dose dexamethasone to an early close and also recommended patients be transitioned to a Revlimid/LDD regimen.

Based on these findings by the two cooperative groups, The International Myeloma Foundation's U.S. Myeloma Forum, a committee of the nation's leading myeloma experts, is considering the first large, inter-group trial for newly-diagnosed patients using novel agents (either Revlimid with low-dose dexamethasone or Revlimid plus other agents such as Velcade with low-dose dexamethasone) without front-line transplant.

"This is an important series of steps for myeloma patients, as we now have regimens that are more tolerable and at the same time may be more effective," said Brian Durie, chairman and co-founder of the IMF and co-chairman of the SWOG myeloma committee. "Based on this new clinical evidence, we believe that regimens that include Revlimid with low dose steroid are an important option for patients with myeloma at all stages of the disease."

Susie Novis, president and co-founder of the IMF, added, "These findings are particularly exciting because the use of low dose dexamethasone was proposed by patients themselves, showing how much can be achieved when we empower patients and listen to what they have to say. In addition, closer cooperation between the two large cooperative groups, SWOG and ECOG, will provide important benefits to patients."

*Acute Leukemias:*

## Blood Test Could Help In Making Treatment Decisions

(Continued from page 1)

Anderson between 1995 and 2005. The statistics showed significant differences in survival rates in multiple analyses.

The results from the study showed that AML patients who had a low lymphocyte count on day 15 of treatment had a five-year overall survival chance of only 28 percent. However, patients with higher lymphocytes on day 15 had a much better overall survival rate of 85 percent.

For patients with ALL, the most common form of childhood leukemia, researchers found that those children and young adults with a high ALC count on day 15 had an 87 percent six-year overall survival rate while those with a low lymphocyte count had a 55 percent overall survival rate.

Researchers at the Children's Cancer Hospital plan to continue their study by following newly diagnosed patients and have begun a new study that analyzes the subsets of lymphocytes to see which ones have the most impact on prognosis. They hope their findings will be used to help physicians worldwide make decisions on how aggressively to treat their patients.

"Many developing countries lack the latest technologies and treatment options that we have here in the United States," said senior author Patrick Zweidler-McKay, assistant professor of pediatrics. "A complete blood count test is a universal, inexpensive test. There is the potential for physicians worldwide to look at the ALC count to help determine whether the patient needs additional treatment options that aren't available in every center."

In addition to pediatric acute leukemias, these researchers have found that ALC predicts survival in young patients with non-Hodgkin's lymphoma and a bone cancer, Ewing's sarcoma. These findings suggest that this simple test, may redefine the way physicians treat a range of different cancers.

## Phase II Study Finds Dasatinib May Overcome ALL Resistance

The results of a 36-patient phase II clinical trial indicate that the multitargeted drug dasatinib (Sprycel) may be extremely beneficial in adult patients with a form of acute lymphoblastic leukemia (ALL) who have developed resistance or do not respond to another targeted agent, imatinib (Gleevec). The drug's effectiveness did not appear to be hampered by most of the mutations in a key protein that have been associated with imatinib resistance.

Patients in the trial had a specific chromosomal translocation, often referred to as the Philadelphia chromosome, that is associated with a rapid course of disease after ALL diagnosis and poor survival. The translocation creates a fused protein known as BCR-ABL, the same protein typically seen in chronic myelogenous leukemia, for which imatinib has proven to be an effective treatment.

"These data are highly significant given the refractory nature of patients enrolled in this trial to current treatment modalities, including imatinib," wrote study leader Olivier Ottmann from Johann Wolfgang Goethe University in Germany and colleagues in a May 11 early online release in Blood.

In the study, patients given dasatinib at 70 mg twice daily had strong hematologic and cytogenetic response rates—a return of normal white blood cell counts and a significantly reduced number of cells positive for the Philadelphia chromosome, respectively. At 8 months, 42 percent of patients had a major hematologic response, of whom two-thirds exhibited no disease progression; 58 percent of patients had complete cytogenetic responses.

*Sarcoma:*

## Sarcoma Survivors At Risk Of Blood Clots, Study Finds

NCI researchers have determined that children and young adults with sarcoma are at increased risk of having a thromboembolic event (TE) in their veins. Thromboembolic events involve a blood clot in a vessel that can interfere with normal blood flow.

Clots can sometimes breaks loose and travels through the blood stream to form new clots at locations in the body where they can be life-threatening. TEs are almost always treatable if detected early.

The study investigators also found that pediatric patients whose cancer had spread beyond the original cancer site were more likely to develop a TE than those with localized cancer. These findings are from a study reported in the April 20 issue of the Journal of Clinical Oncology. Researchers reviewed patient records for 122 children and young adults treated for sarcoma in the Pediatric Oncology Branch of the NCI between October 1980 and July 2002.

The study results showed that, over the 22-year

study period, 16 percent of children and young adults with sarcoma developed a TE. However, the researchers noted that this figure probably underestimates the true frequency of TEs in this pediatric patient population. Since this was a retrospective study of archival patient records, most of the original physicians may not have specifically looked for TEs, so some blood clots would have gone unrecorded. Also, TEs often are asymptomatic and early screening was less accurate. As the study observed, the rate at which TEs were detected in sarcoma patients increased from 7 percent before 1993 to 23 percent since 1993, which they attributed to improved screening techniques.

Children whose cancer had spread to other parts of the body were 2.5 times more likely to develop a TE than those whose disease was localized. The most common locations of the blood clots were in the deep veins of the legs and arms, the lungs (pulmonary embolism), and the inferior vena cava, which is the large vein that carries blood from the lower half of the body to the heart. Of the patients who developed a TE, 40 percent had no symptoms related to their blood clot. Thromboses were often detected around the same time as the cancer diagnosis.

Previous research had shown a link between cancer and TEs in adults, but data regarding TEs in adults may not be applicable to children with cancer. Children differ from adults in the types of cancer that occur, as well as in the number and types of co-morbid conditions. The researchers only looked at sarcomas (cancers of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue) in children, so not all pediatric cancer types were represented. Sarcomas account for 15 to 20 percent of pediatric cancers and include rhabdomyosarcoma, Ewing sarcoma, and osteosarcoma. Approximately two-thirds of these cases can be cured.

A total of 23 TEs occurred in 19 of the 122 patients during the 22-year period of record keeping. Twenty-three percent of patients with metastatic cancer developed a TE, compared to 10 percent of patients with localized cancer, suggesting an association between tumor burden and the risk of TE.

"Children and young adults with sarcoma should be closely monitored for thrombosis because these patients may not have any symptoms related to a TE and because thromboembolism is a potentially life-threatening complication that is almost always amenable to therapy," said Alan Wayne, clinical director of NCI's Pediatric Oncology Branch at the Center for Cancer Research.

*Lymphoma:*

## Risk of Lymphoma Increases with Hepatitis C Virus Infection

People infected with the hepatitis C virus (HCV) are at an increased risk of developing certain lymphomas (cancers of the lymphatic system), according to a study published in the May 8 issue of the Journal of the American Medical Association.

Researchers from NCI and Baylor College of Medicine found that HCV infection increased the risk of developing non-Hodgkin's lymphoma by 20 percent to 30 percent. The risk of developing Waldenström's macroglobulinemia (a rare type of non-Hodgkin's lymphoma) went up by 300 percent and the risk for cryoglobulinemia, a condition marked by abnormal levels of certain antibodies in the blood, was also elevated for those with HCV infections.

The researchers looked at patient records collected from Veterans Affairs hospitals between 1996 and 2004. Researchers selected more than 700,000 records; 146,394 represented patients who were diagnosed with the hepatitis C virus, while 572,293 represented patients who were not. Based on that review, researchers determined, first, that the patients infected with HCV had a higher risk of developing lymphoma and, second, that HCV infection preceded development of the lymphoma. The risk of lymphomas in HCV-infected patients was charted across more than five years of follow-up.

"This is one of the largest studies ever conducted to look at the relationship between hepatitis C virus infection and cancers of the lymphatic system," said NCI Director John Niederhuber. "Since so much is still unknown about the causes of lymphoma, establishing which factors contribute to the disease is the first step in finding ways to reduce its incidence and lessen mortality."

HCV causes hepatitis, which is an inflammation of the liver. The HCV virus is carried through the blood and is passed from person to person through the exchange of bodily fluids -- via shared needles, open wounds, and sexual contact, among other means. HCV is also known to cause cirrhosis and liver cancer.

"Although the risk of developing lymphomas is small, our research suggests that screening of HCV-infected individuals could identify conditions which may lead to cancer. It might then be possible to prevent progression to lymphoma," said investigator Eric Engels, from the Viral Epidemiology Branch of NCI's Division of Cancer Epidemiology and Genetics. "More research is needed to further clarify the relationship

between HCV infection and lymphoma."

The researchers note that this study was limited to military veterans who used the VA system, so the results may not be applicable to the overall U.S. population. The study population was mostly men (97 percent), the majority of patients were white, and the average age was 52 years. Patients in the HCV-infected group were more likely to have served during the Vietnam era (1964-1975) than were uninfected patients in the comparison group.

Previous studies found that the prevalence of HCV infection is much higher among U.S. veterans who use the VA medical system (5 percent) than in the general population, where only 1.6 percent carry the virus. Several factors have likely contributed to this higher prevalence, including demographics, socioeconomic status, and particularly a history of injection drug use or blood transfusions received before 1990, when screening for hepatitis C virus was started.

This study was funded in part by NCI's Intramural Research Program and the Michael E. DeBakey Veterans Affairs Medical Center in Houston, Texas.

*Cervical Cancer:*

## Long-Term Results Find Cisplatin Improves Survival

Long-term follow-up results from a Gynecologic Oncology Group clinical trial that compared cisplatin-based chemotherapy with hydroxyurea in addition to radiation therapy for locally or regionally advanced cervical cancer, published online in the Journal of Clinical Oncology, showed that cisplatin-based chemotherapy significantly improved both progression-free and overall survival compared with hydroxyurea alone.

The percentage of women experiencing late side effects did not significantly differ between the treatment groups.

The investigators randomly assigned participating women to one of three groups. One group received cisplatin alone, the second received the chemotherapy drug hydroxyurea alone, and the third received a combination of cisplatin, hydroxyurea, and the drug 5-fluorouracil (5-FU).

All drugs were given during radiation therapy, and all women received the same type and amount of radiation therapy.

Patients were followed for an average of almost 9 years. Women who received either cisplatin or the combination of cisplatin, 5-FU, and hydroxyurea had significantly longer progression-free survival and overall survival than women who received hydroxyurea alone, regardless of whether the cancer had spread locally or regionally.

After adjusting for the fact that more patients who received cisplatin or the combination regimen were alive for the analysis of side effects, the investigators did not observe a significant difference in late-occurring side effects between the groups.

"Collectively, this follow-up analysis continues to support the use of cisplatin-based concurrent chemotherapy with pelvic radiation therapy for locally advanced stage cervical cancer," summarized the authors.

*Ovarian Cancer:*

## Study Links Ovarian Cancer To Hormone Replacement

Women who use hormone replacement therapy have an increased risk of developing ovarian cancer and dying from the disease, a large British study reported.

The risk increases the longer HRT is used, but risk returns to the level seen in women who have never used hormones, once HRT is stopped. The participants were from the Million Women Study, and about 500,000 of the women had taken HRT.

Women who were currently using HRT were on average 20 percent more likely to die from ovarian cancer than those who had never received HRT. Since 1991, the researchers estimate, HRT use has led to an additional 1,000 deaths from ovarian cancer, as well as an additional 1,300 new diagnoses of ovarian cancer in the United Kingdom.

The findings should be considered along with studies linking HRT use to endometrial and breast cancers, the researchers say. The incidence of these three cancers in the study population was 63 percent higher in current users of HRT than in never users, according to findings published online in The Lancet on April 19.

"When ovarian, endometrial, and breast cancer are taken together, use of HRT results in a material increase in the incidence of these common cancers," wrote Valerie Beral of the Epidemiology Unit at Cancer Research UK in Oxford and her colleagues.

Although use of HRT has declined greatly in recent years, enormous numbers of women have been exposed. "With these new data on ovarian cancer, we expect the use of HRT to fall further," said Steven Narod of Women's College Research Institute, Toronto, in an accompanying editorial.

*Cancer Prevention:*

## Smokers Who Quit Live Longer Than Those Who Spit—Study

An American Cancer Society study of more than 116,000 men finds that cigarette smokers who switched to spit tobacco products had a higher risk of dying prematurely from tobacco-related diseases than former smokers who stopped using all forms of tobacco.

The study is the first to compare death rates among those who quit using tobacco entirely with those who switch. Previous studies have examined morbidity and mortality among the two groups separately but have not compared them.

In the study, Jane Henley and colleagues from ACS and Centers for Disease Control and Prevention's Office on Smoking and Health used data from the Cancer Prevention Study II (CPS-II) to compare tobacco-related disease among male smokers who quit using tobacco entirely to men who quit smoking cigarettes but switched to using spit tobacco. The authors also compared mortality rates of men who never used any tobacco products to those of switchers and smokers who quit using tobacco entirely.

The study's principal finding was that the men who switched from smoking cigarettes to using spit tobacco had higher death rates from lung cancer, stroke, heart disease and all causes combined than men who quit using tobacco entirely. Switchers also had more than twice the death rate from cancers of the mouth and throat.

*FDA Approvals:*

## FDA Approves New Drug for Advanced Kidney Cancer

FDA approved Torisel (temsirolimus) for the treatment of a certain type of advanced kidney cancer known as renal cell carcinoma. Torisel was approved based on a study that showed use of the drug prolonged survival of patients with renal cell carcinoma. The drug is an enzyme inhibitor, a protein that regulates cell production, cell growth and cell survival.

"We have made significant advances in the battle against kidney cancer," said Steven Galson, director of the FDA's Center for Drug Evaluation and Research. "Torisel is the third drug approved for this indication in the past 18 months, and one that shows an increased time in survival for some patients."

The approval of Torisel follows the December 2005 approval of Nexavar (sorafenib), which was based on a delay in progression of disease. In January 2006, Sutent (sunitinib) received accelerated approval based on durable response rate, or tumor size reduction, and was later demonstrated to delay tumor progression.

The safety and effectiveness of Torisel were shown in a clinical trial of 626 patients divided into three groups. One group received Torisel alone, another received a comparison drug called Interferon alfa, and a third received a combination of Torisel and interferon.

The group of patients who received Torisel alone showed a significant improvement in overall survival. The median overall survival was 10.9 months for patients on Torisel alone versus 7.3 months for those treated with the interferon alone. Progression-free survival (when the disease does not get worse) increased from 3.1 months on the interferon alone arm to 5.5 months on the Torisel alone arm. The combination of Torisel and interferon did not result in a significant increase in overall survival when compared with interferon alone.

The most common adverse reactions, occurring in at least 30 percent of Torisel-treated patients, were rash, fatigue, mouth sores, nausea, edema, and loss of appetite. The most common laboratory abnormalities were high blood sugar, elevated blood lipids and triglycerides, elevated liver and kidney blood tests, and low red cell, white cell, and platelet counts.

Torisel is manufactured by Philadelphia-based Wyeth Pharmaceuticals Inc.

## FDA Approves New Indication For Anticoagulant Frangmin

FDA has approved a new indication for the anticoagulant Frangmin (dalteparin sodium injection) for the extended treatment of symptomatic venous thromboembolism and/or pulmonary embolism to reduce the recurrence of VTE in cancer. The agent is the first low-molecular-weight heparin approved in the U.S. for the indication.

Data from the CLOT study showed Fragmin reduced the recurrence of blood clots in cancer by 50 percent compared to standard anticoagulant therapy, the company said. "Cancer treatments and the disease itself put this patient population at significantly higher risk than non-cancer patients for developing DVT or PE, the two conditions described as VTE," said Frederick Rickles, clinical professor of medicine at George Washington University Medical Center and a CLOT study investigator.

The CLOT trial evaluated the safety and efficacy of Fragmin in reducing the recurrence of DVT/PE in patients with cancer, compared to an oral anticoagulant.

Patients with acute DVT, PE or both were randomized into two groups of 338 each. One group received the drug for six months. The other group received Fragmin for five to seven days, followed by Warfarin for six months. The study showed that, during a six-month period, nearly twice as many patients (53) treated with Warfarin experienced at least one episode of DVT or PE compared to those treated with a once-daily administration of Fragmin (27). Most of the difference occurred during the first month of treatment. The benefit was maintained over the six-month study period. Mortality rates were similar between the study groups at the end of the study. The safety findings were numerically higher for the Fragmin group versus the Warfarin group for major bleeding, thrombocytopenia and liver enzyme elevations, the company said.

Fragmin is a registered trademark of Pfizer Health AB and is licensed to Eisai Inc.

## NCI-Approved Group, Center Clinical 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/II**

Phase I-II Study of R115777 (Tipifarnib (Zarnestra ) Plus Sequential Weekly Paclitaxel Followed by Dose-Dense Doxorubicin and Cyclophosphamide in Patients with Stage IIB-IIIC Breast Cancer. Montefiore Medical Center, protocol 7868, Hershman, Dawn, phone 212-305-1945.

Phase II Study of Gemcitabine, Paclitaxel, and Doxorubicin, with Pegfilgrastim for the Treatment of Patients with Metastatic Transitional Cell Carcinoma and Renal Insufficiency. M D Anderson Cancer, protocol 7341, Pagliaro, Lance, phone 713-792-2830.

Phase II Safety and Efficacy Study with the VEGF Receptor Tyrosine Kinase Inhibitor GW786034 in Patients with Inhibitor GW786034 in Patients with Metastatic Urothelial Cancer. Mayo Clinic Rochester, protocol 7661, Pili, Roberto, phone 410-502-7482.

Phase II Study of Imatinib Mesylate in Patients with Inoperable AJCC Stage III or IV Melanoma Harboring Somatic Alterations of c-KIT. Memorial Sloan-Kettering Cancer Center, protocol 7754, Schwartz, Gary, phone 212-639-8324.

Phase II Study Trastuzumab in Her2/neu Positive Cancer of the Gallbladder or Biliary Tract. M D Anderson Cancer Center, protocol 7756, Thomas, Melanie, phone 713-792-2828.

Phase II Study of Dasatinib in Patients with Metastatic Adenocancinoma of the Pancreas. Case Western Reserve University, protocol 7828, Brell, Joanna, phone 216-844-5413.

Randomized Phase II Study of Vorinostat or Placebo in Combination with Carboplatin and Paclitaxel for Patients with Advanced or Non-Small Cell Lung Cancer. City of Hope National Medical Center, protocol 7863, Ramalingam, Suresh, phone 412-648-6619.

Phase II Study of Dasatinib in Patients with Chemo-Sensitive Relapsed Small Cell Lung Cancer. Cancer and Leukemia Group B, Protocol CALGB-30602, Ramnath, Nithya, phone 716-845-3099.

**Phase III**

Assessment of Topical Treatment Response with Amitriptyline and Ketamine: Combination Trial in Chemotherapy Peripheral Neuropathy. University of Rochester, protocol URCC-06-05, Dworkin, Robert, phone 585-275-3524.

**Other**

COG Study for Collecting and Banking Ewing Sarcoma Specimens. Children's Oncology Group, protocol AEWS07B1, Lessnick, Stephen, phone 801-585-9268.

Identification of Biomarkers in Follicular Lymphoma. Eastern Cooperative Oncology Group, protocol E1496T1, Horning, Sandra, phone 650-725-6456.

Development of a Model to Predict Progression Free Survival After Treatment with Erlotinib in E3503. Eastern Cooperative Oncology Group, protocol E3503T1, Kolesar, Jill, phone 608-262-5549.

**Pilot**

Safety and Immunogenicity of Vaccination with Multi-Epitope Peptide Vaccine Containing MART-1, gp100, and Tyrosinase Peptides Given with the Combination of GMCSF and CpG Oligonucleotide (CpG 7909) in ISA-Oil Adjuvant for Patients with Recurrent Inoperable Stage III or Stage IV Melanoma. University of Pittsburgh, protocol 7357, Kirkwood, John, phone 412-623-7707.

Pilot Study of Lestaurtinib (CEP-701) in Combination with Chemotherapy in Refractory FLT3-Mutant Acute Myeloid Leukemia. Children's Oncology Group, protocol AAML06P1, Young, Patrick, phone 410-614-4915.