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THE
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Cancer research news for clinicians

American Society of Hematology Meeting:

Dasatinib, Nilotinib Show Strong Early Results As Frontline Therapy For CML

Two drugs approved for use as second line therapy for chronic myelogenous leukemia are showing promising results as frontline therapy for newly diagnosed patients in two clinical trials, research teams led by scientists at M. D. Anderson Cancer Center said at the annual meeting of the American Society of Hematology.

All patients in both trials have a complete cytogenetic response—absence of the aberrant chromosome that causes the disease—after one year on either drug. Approximately 90% reach complete cytogenetic response as early as 6 months.

"These are early results but certainly encouraging so far in both cases,"

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Breast Cancer:

Accuracy Of Diagnostic Mammograms Varies By Radiologist, Study Finds

For women with breast symptoms such as lumps, the ability of diagnostic mammograms to detect breast cancer accurately depends strongly on which radiologist reads them, according to a Group Health study published online on Dec. 11 in the Journal of the National Cancer Institute.

"When a woman gets a mammogram, she wants to know that if she has breast cancer, the mammogram will be likely to detect it," said study leader Diana Miglioretti, an associate investigator at Group Health Center for Health Studies. "This is especially important when the woman has a breast concern such as a lump."

Ideally, this ability to accurately detect cancer (known as "sensitivity") would be consistently high, with few false-positives—biopsies performed despite the absence of cancer. And it wouldn't depend on which radiologist was reading the mammograms. "But that's not what we found," she added.

The research team examined how well 123 radiologists interpreted nearly 36,000 diagnostic mammograms done to evaluate breast problems, such as lumps, from 1996 through 2003 at 72 U.S. facilities, including six from Group Health, that contribute data to the Breast Cancer Surveillance Consortium.

For different radiologists, sensitivity ranged from 27 percent to 100 percent; and false-positives, from 0 to 16 percent. These differences were only

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Sprycel, Tasigna Improve Response In CML, Study Finds

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said lead author Jorge Cortes, professor in M. D. Anderson's Department of Leukemia. Patients in both trials are in the chronic, or initial phase, of CML and had not received prior therapy for their disease.

The two medications are dasatinib, the Bristol-Myers Squibb drug known as Sprycel, and nilotinib, the Novartis drug known as Tasigna. Both have been approved by FDA for use in CML patients whose disease becomes resistant to the frontline therapy imatinib, also a Novartis drug known as Gleevec, or who become intolerant to the drug.

Cortes and colleagues compared the two medications at 3, 6 and 12 months with historical data from patients who took either 400 mg or 800 mg daily of Gleevec.

For dasatinib, at three months 26 of 33 patients (79%) achieved complete cytogenetic response. At six months 30 of 32 (94%) and at 12 months all 24 evaluable patients were at a complete cytogenetic response.

For nilotinib, at three months 21 of 22 patients (95%) achieved complete cytogenetic response with all 13 evaluable patients at six months and all 11 at 12 months reaching complete cytogenetic response.

Historical complete cytogenetic responses for low-dose imatinib were 37% at three months, 54% at six months and 65% at a year. For high-dose imatinib the historical response rates were 62%, 82% and 86%.

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As frontline treatment, imatinib has increased the 5-year survival rate for CML patients from 50% to 90%. Imatinib targets the aberrant Bcr-Abl protein, caused by a chromosomal abnormality called the Philadelphia Chromosome, which fuels an overabundance of white blood cells and immature stem cells called blasts that crowd out red blood cells and platelets.

Nilotinib and Dasatinib target a greater variety of genetic variations leading to CML than does imatinib.

Both clinical trials continue to enroll patients. Side effects are being closely monitored and some patients in each trial had their doses reduced or treatment temporarily interrupted to deal with toxicities. "We can't say at this moment that either drug has major problems with side effects," Cortes said.

"As some of our patients started to develop resistance to imatinib, we started searching for agents to bypass that resistance, working with the pharmaceutical companies to test new agents," said Hagop Kantarjian, chair of M. D. Anderson's Department of Leukemia.

Kantarjian developed, designed and conducted the clinical trials that led to approval of nilotinib by the FDA last month for patients who can no longer take imatinib.

Moshe Talpaz developed, designed and conducted clinical trials that led to approval of dasatinib by the FDA in June 2007 for the same group of patients. Talpaz is now at the University of Michigan.

Cortes is leading research into a third drug, bosutinib, produced by Wyeth Pharmaceuticals, as a second-line therapy for CML.

"We now have enough tools to allow the vast majority of CML patients to live a normal life," said Kantarjian. "And we are always searching for better alternatives."

Current drugs successfully target all mutations that cause CML except for one, known as the T3151 variant. "We're looking at other agents to tackle that one," Kantarjian said.

Oblimersen Combination Improves CLL Survival

Relapsed chronic lymphocytic leukemia patients who had a complete response to combination therapy that included the drug oblimersen (Genasense) survived significantly longer than patients treated with chemotherapy alone, a team led by researchers at M. D. Anderson Cancer Center reports at the annual meeting of the American Society of Hematology.

Patients who achieved a complete response with

oblimersen have survived so well that a median survival time cannot yet be calculated, but it is estimated to exceed 49 months. Those who achieved complete response with chemotherapy alone had a median survival time of 35 months.

"In a relapsed population, that's excellent survival," said lead author Susan O'Brien, professor in M. D. Anderson's Department of Leukemia. "Survival is associated with achieving complete response."

The phase III clinical trial compared a regimen of fludarabine and cyclophosphamide (F/C) with F/C plus oblimersen. Oblimersen blocks the Bcl-2 protein, which plays a critical role in progression of chronic lymphocytic leukemia, including development of resistance to treatment.

By stifling Bcl-2, researchers believe CLL becomes more vulnerable to chemotherapy such as the F/C combination.

In a paper published in the Journal of Clinical Oncology in March, O'Brien and colleagues showed that patients who received the oblimersen combination were more likely to have a complete response (20 out of 120 patients, or 17%, compared to 8 out of 121 patients, 7%, who received only the F/C chemotherapy).

Complete response was more durable in the oblimersen-treated patients, with a median duration of at least 36 months compared with 22 months for those on F/C alone.

The question unanswered by the JCO paper was whether this advantage in complete response translated into an advantage in survival, O'Brien said.

Patients were followed for at least three years after randomization or until death or withdrawal from the study. Of the 20 oblimersen-treated patients with a complete response at the end of the first year, 12 survived at least four years. Of the eight complete responders in the other group, four survived at least four years.

The survival data confirm that complete response is a valid endpoint for clinical trials in relapsed or resistant CLL, O'Brien said.

Evidence Links Anemia Drugs With Leukemic Transformation

Mayo Clinic researchers reported the discovery of a link between erythropoiesis-stimulating agents (ESAs) and leukemic transformation (conversion to leukemia) of the blood disorder myelofibrosis.

The results of the retrospective study, which sought to quantify the risk factors for leukemic transformation, were presented by lead author Jocelin Huang at the American Society of Hematology's annual meeting.

"We believe this to be the first large systematic evaluation of the risk factors leading to leukemic transformation in primary myelofibrosis," said Huang, hematology researcher at Mayo Clinic.

The researchers confirmed a number of clinical and laboratory variables that appeared to correlate with leukemic transformation. Independent risk factors for development of leukemia included peripheral blood blast (immature leukemia cells) levels greater than or equal to 3 percent; and a platelet count of less than 100x109/liter. The more surprising findings were that specific treatments also appeared to be related to leukemic transformation. Use of ESAs or danazol (a hormone with anemia-countering properties) were linked to later development of leukemia, independent of the blast or platelet levels.

Ayalew Tefferi, principal investigator of the study, and a Mayo Clinic hematologist, said the findings are based on retrospective observation and need to be validated in properly designed prospective studies. "While we cannot take these findings as an absolute, at the same time, they cannot be ignored," Tefferi said. "Treatment decisions regarding the use of ESAs in patients with primary myelofibrosis should carefully be evaluated."

ESA treatment in patients with primary myelofibrosis has the potential to cause further enlargement of the spleen, he said.

The study evaluated the records of 311 Mayo Clinic patients seen with primary myelofibrosis between 1976 and 2006. Of these patients, at an average follow-up of 27 months, 27 cases (9 percent) of leukemic transformation were documented.

Other factors appeared to contribute to the development of leukemia, including anemia, leukocytosis and peripheral blood monocyte count greater than or equal to 1x109/L (both are measures of elevated white blood cells), hypercatabolic symptoms (results of excess metabolism), a splenectomy and treatment with androgens (a type of hormones). However, they were not independent predictors.

Primary myelofibrosis, also called myelofibrosis, is a bone marrow disorder that disrupts the body's normal production of blood cells, and results in scarring in bone marrow. The scarring leads to anemia and enlargement of the spleen and liver. Myelofibrosis is characterized by an overproduction of white blood cells. While the mechanism is not precisely understood, the scarring (fibrosis) of the bone marrow is thought to be a reaction to the activity of these excess white blood cells.

Breast Cancer:

Accuracy Of Mammogram Readings Varies, Study Finds

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partially explained by the characteristics of the patients and the experience of the radiologists.

The radiologists who read diagnostic mammograms most accurately (with highest sensitivity, without too many false-positives) tended to be those who were based at academic medical centers or spent at least 20 percent of their time on breast imaging. By contrast, unlike in Europe, most U.S. women get mammograms interpreted by general radiologists who interpret mammograms as only a small percentage of their practice.

"We need to reduce the wide variability among radiologists in how they interpret diagnostic—and screening—mammograms," said Miglioretti. "A good way to do that may be to identify the radiologists who are least accurate at reading mammograms—and to improve their performance with extra training."

The national Breast Cancer Surveillance Consortium is working on ways to accomplish these goals, including developing an interactive training program.

"Women should get regular screening mammograms," said Miglioretti. "Mammography isn't perfect, but it's the best way we have to detect breast cancer early, when it has the greatest chance of being cured." She also urged women with breast concerns, such as lumps, to try to get evaluated at a center that has at least one breast imaging specialist: a radiologist who spends a large percentage of the time reading mammograms and performing breast biopsies.

Most mammograms are done to screen women with no symptoms for breast cancer. Previous research has shown that radiologists vary widely in how they read such screening mammograms. This new study is the largest to examine what predicts variability in diagnostic mammograms.

Stereo Mammography Detects More Lesions, Study Finds

A new radiological diagnostic tool called stereo mammography allows clinicians to detect more lesions and could significantly reduce the number of women who are recalled for additional tests following routine screening mammography.

The findings from a clinical trial underway at Emory University were presented at the annual meeting of the Radiological Society of North America.

In the study, stereoscopic digital mammography reduced false-positive findings by 49 percent compared to standard digital mammography, and reduced missed lesions by 40 percent, according to Carl D'Orsi, professor of radiology, Emory University School of Medicine, and director of breast imaging.

"This finding is very significant because it shows the technology cuts by almost half the number of women who are recalled for additional tests, reduces the number of false positives that typically occur in standard mammograms and eliminates significant anxiety in patients and their loved ones," D'Orsi said.

"Standard mammography is widely considered to be one of the most difficult exams to read because lesions may be disguised by normal tissue," D'Orsi said. "At the same time, false-positives can also occur because of the two dimensional images provided by the existing technology."

Stereo mammography consists of two digital x-ray images of the breast acquired from two different points of view separated by about eight degrees. When the images are viewed on a stereo display workstation, the radiologist is able to see the internal structure of the breast in three dimensions.

In the study, researchers use a full-field digital mammography unit modified to take stereo pairs of images. A stereo display workstation allows the mammographer to fuse the stereo image pair, while viewing the breast in depth.

As of July 2007, 1,093 patients at elevated risk for developing breast cancer were enrolled in the clinical trial. Each patient received a full-field, standard digital mammography screening examination and a full-field, stereoscopic digital exam. The exams were read independently by different radiologists. A total of 259 suspicious findings were detected by the combined mammography procedures and were referred for additional diagnostic testing, including biopsy when indicated. Of those, 109 were determined to be true lesions. Standard mammography missed 40 of the 109 lesions while the stereoscopic exam failed to detect 24, a 40 percent decrease in missed lesions.

According to the researchers, increasing the use of stereo mammography at many institutions across the country would require simple upgrades to existing digital mammography equipment and software. The stereo digital exam currently takes the same amount of time to read as a standard mammogram, and researchers are working toward making radiation exposure in stereo scans comparable.

MRI Reveals Information That May Alter Treatment

In about 20 percent of women with breast cancer who plan to undergo a lumpectomy, breast magnetic resonance imaging reveals important diagnostic information that alters their treatment plan, University of Florida surgeons have found.

MRI, which is not routinely administered to these patients, can find additional cancerous areas in the breast that previously evaded detection, discover cancer in the opposite breast that standard imaging tests such as mammography and ultrasound missed, or determine a tumor is actually larger than expected, the doctors said.

Some of these women end up needing a total mastectomy instead of breast-conserving lumpectomy. Others whose tumors are bigger than indicated on standard imaging could be less likely to face a second operation to remove cancerous cells left behind after a tumor is removed if MRI findings signal the need for surgeries to be more aggressive.

Either way, UF surgeons said MRI can help confirm which women are indeed candidates for a breast-sparing operation.

"In these patients, we did one of three things: We offered them a mastectomy, we offered them another treatment—preoperative chemotherapy to shrink the lesion and allow us to save the breast—or, in some cases, we could perform a more precise excision to remove the cancer," said Stephen Grobmyer, an assistant professor of surgical oncology and endocrine surgery in the UF College of Medicine's department of surgery.

"When you operate for breast cancer, you need to achieve clear margins around the tumor," he said. "This inability to clear the margin is a problem that continues to plague both breast surgeons and patients. In some recent reports the margin-positive resection rate for breast cancer is up to 50 percent."

Findings from the UF study, a retrospective review of 79 women ages 29 to 82 who had localized noninvasive or early stage invasive breast cancer and were planning to have a lumpectomy, were presented at the Southern Surgical Association's annual meeting in Hot Springs, Va. Study participants had undergone preoperative MRI—which provides highly detailed images of the breast, particularly in women whose breast tissue is very dense—for diagnostic purposes and, when indicated, MRI-directed biopsies for preoperative evaluation of suspicious areas between January 2006 and July 2007.

"We're talking about MRIs for patients who have breast cancer and would like to save the breast, to make sure there is [no other cancer] in the breast that would eliminate them from breast conservation," said Edward Copeland III, the Edward R. Woodward professor of surgical oncology and endocrine surgery at UF.

Until now, few studies have focused on the use of breast MRI for confirmation of the extent of disease in patients already found to have cancer through traditional imaging methods. Recommendations published earlier this year in the New England Journal of Medicine touted the merits of annual breast MRI for screening women with a high lifetime risk of breast cancer because of family history or their genetic makeup, but did not advocate widespread use.

In the UF study, 21 patients underwent an MRI-guided biopsy after preoperative breast MRI revealed a suspicious area. About 40 percent of the biopsies revealed additional cancer. The MRI led to a change in treatment plan in 19 percent of the study sample. Overall, approximately three-fourths of patients underwent a partial mastectomy, also known as lumpectomy or breast-conserving surgery, while one-fourth ultimately had a total mastectomy, said UF's chairman of surgery William Cance.

UF surgeons say high-quality preoperative breast MRI along with the capacity to perform MRI-guided biopsy could benefit many cancer patients because it detects cancers that otherwise would be missed, particularly women with dense breasts that are difficult to see on mammography or smaller lesions hard to pinpoint on ultrasound. Early diagnosis and treatment of other sites of breast cancer with MRI may reduce recurrence rates following treatment, said Grobmyer, who is affiliated with the UF Shands Cancer Center.

"MRI has been known for a while to be the most sensitive method to detect breast cancer," Grobmyer said. "Some concerns over the use of MRI in this context have been one, the cost, and two, the fact that MRI detects many 'abnormal' areas that upon further work-up turn out not to be cancer."

The cost of breast MRI can run 10 times that of mammography. That and subjecting women to the anxiety and discomfort of a biopsy for a tumor that turns out to be benign are among the reasons why using MRI has not been advised for everyone.

Still, if larger studies show that preoperative MRI reduces the need for second operations to obtain clean margins, some or all of the cost of the imaging could be offset by savings from avoiding more surgery, Grobmyer said. Costs may also be offset by reducing the future

need for operations to manage breast cancer recurrences, which Grobmyer believes will be reduced by the use of preoperative MRI.

Other research will have to answer whether by identifying cancerous areas earlier and changing the treatment plan, patients will have lower recurrence rates and improved cancer-related survival.

UF researchers said MRI might be especially useful for people considering partial breast radiation therapy. Patients undergoing lumpectomy typically receive whole-breast radiation, but more recently some practitioners have opted to only radiate a portion of the breast because when cancer recurs it typically does so in the scar from the original surgery, Grobmyer said.

"There is some suggestion that the recurrence rate in these patients is fairly low, but we're worried this finding of breast cancer at other sites of disease is particularly important in patients considering partial radiotherapy," he said. "Our study certainly raises questions—should you do MRI before you consider partial breast radiotherapy to make sure you don't have disease in other sites of the breast?"

Race, Age Play Role In Delay Of Surgery For Breast Cancer

Race and age appear to play a role in how quickly a woman newly diagnosed with breast cancer is surgically treated, with a lengthy delay potentially impacting overall survival, report researchers at Johns Hopkins Medical Institutions.

Factors such as socioeconomic status and the cumulative effects of a patient's other illnesses likely contribute to these delays, according to the study, presented at the American Association for Cancer Research International Conference on Frontiers in Cancer Prevention Research, held earlier this month in Philadelphia.

Preliminary results of the study of 1,477 patients show that the average interval from breast cancer diagnosis to surgery was six days longer for African-American women than for Caucasian women. Women who were older than age 70 had an average interval of 12 more days than women younger than 40.

The researchers also observed that the women who experienced an interval of more than 60 days between diagnosis and treatment were 1.8 times more likely to have died from any cause when compared to women who had their surgery within 60 days of diagnosis. In this study, the average interval from diagnosis to surgery for all patients was 29 days.

"We think that timely treatment could make difference in patient care," said Hae Seong Park, a research coordinator in the Department of Oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

As the study is based on the registry data from a single institution, further research is necessary to confirm the findings and to generalize the results. All of the patients had surgery—either a lumpectomy or mastectomy—between 2000 and 2005 at Johns Hopkins Hospital, including those who had a diagnostic biopsy at a different institution.

The researchers found that on average, Caucasian women were treated 28 days from diagnosis, compared to 34 days for African-American women. On average, women younger than 40 were treated within 21 days; patients 40-50 were treated within 28 days; women in their 50s were treated within 31 days; patients 60-70 were treated by 29.5 days after diagnosis; and women over age 70 had an average treatment interval of more than 33 days.

Investigators also looked at the place and year of diagnosis and found that the shortest interval, 24 days on average, occurred during 2000-2001; and the longest was 2002-2003 when the average interval was 34 days. Intervals were less in 2004-2005 (almost 30 days).

There were no significant differences in time to treatment based on the stage of cancer that a woman was diagnosed with, Park said.

"Although this is one factor that one might expect a time differential, we did not observe much difference," she said.

Worrisome to the researchers, however, was the finding that almost 24 percent of patients did not receive adjuvant therapy, such as chemotherapy or hormone therapy following surgery.

Preliminary findings suggested that patients who had surgery more than 60 days from diagnosis received adjuvant therapy less frequently. This might be of greater importance, since adjuvant therapy does improve survival, Park said.

"Most patients should have received such treatment, but it may be that the cancer registry data did not reflect all of this information," she said.

The investigators also did not have information on the patients' insurance status or any other data that could explain some of the time lags.

"We plan to review individual patient records and collect more information to confirm what we observed, and perhaps to think about interventions to provide more timely and complete care," Park said.

Weight Gain After Diagnosis Increases Risk Of Death

Gaining weight following a diagnosis of invasive breast cancer could increase a woman's risk of death from the disease by more than half, according to researchers leading the Collaborative Women's Longevity Study.

The researchers associated weight gain with a measurable increase in risk of death due to all causes, not just breast cancer. The study was presented at the American Association for Cancer Research International Conference on Frontiers in Cancer Prevention Research.

"Our findings provide additional support for the benefits of maintaining a healthy weight and exercising," said Hazel Nichols, a doctoral student in the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health. "According to our results, there is a 14 percent increase in risk for every five kilograms—about 11 pounds—of weight gained."

To analyze the effect of weight gain on breast cancer survival, Nichols and her colleagues contacted women who had taken part in one of three previous studies begun in 1988 at sites in Wisconsin, Massachusetts, and New Hampshire. Between 1998 and 2001, Nichols' team surveyed the women about post-diagnosis weight, weight gain, physical activity, diet and related items.

Of the original 4,021 breast cancer patients, the researchers identified 121 breast cancer-related deaths and 428 total deaths. For women classified as obese by body mass index, the risk of dying from breast cancer was nearly 2.4 times that of women classified with a normal body weight. "Obesity was associated with risk of death even after accounting for age, menopausal status or smoking," Nichols said.

Non-Caucasians At Higher Risk For Severe Breast Cancer Pain

Non-whites experience poorer pain control among women with metastatic breast cancer, according to a new study.

Liana Castel of the University of North Carolina at Chapel Hill and co-investigators studied 1,124 women with metastatic breast cancer and bone metastases who received standard treatment in an international chemotherapy clinical trial conducted from October 1998 to January 2001.

The study comprised women in 19 countries; the majority (82%) of non-whites were from the U.S. A test called the Brief Pain Inventory—which is based on a scale of zero to ten in pain severity—was administered repeatedly over a year to determine pain levels. Non-white women reached a pain level of seven or higher significantly earlier during a year of follow-up, compared with white women. Besides race, other predictors for greater pain were inactive performance status and preceding radiation treatment.

The study is published in the Jan. 1 issue of CANCER, a peer-reviewed journal of the American Cancer Society.

Colorectal Cancer:

Diabetes Associated With Greater Risk Of Cancer

Women with diabetes are 1.5 times more likely to develop colorectal cancer than those who do not have the metabolic disorder, according to researchers at the University of Minnesota.

The findings add to the complex body of evidence linking diet and colorectal cancer and also provide new evidence that furthers the understanding of the role of insulin in cancer promotion. The study was presented at the American Association for Cancer Research's Sixth Annual International Conference on Frontiers in Cancer Prevention Research, held earlier this month in Philadelphia.

"Colorectal cancer and type II diabetes share a number of common factors, including obesity, so it is interesting to see the direct line between these two conditions," said Andrew Flood, assistant professor in the Division of Epidemiology and Community Health at the University of Minnesota School of Public Health and the University of Minnesota Cancer Center. "In general, the idea is that if elevated insulin levels create a biochemical environment conducive to cancer growth, it provides one mechanism by which diet and lifestyle can really influence cancer risk."

Flood and his colleagues examined data from a massive screening study called the Breast Cancer Detection Demonstration Project, initiated at 29 centers throughout the U.S. in the 1970s. Flood's team subsequently followed more than 45,000 study participants with no history of colorectal cancer or self-reported diabetes for eight years, (from 1987-1989 and from 1995-1998), to identify which of them subsequently developed colorectal cancer.

According to their findings, women with diabetes had a greatly increased risk of developing colorectal cancer. "These results remained statistically significant even after controlling for all known and suspected confounding variables," Flood said.

It is not exactly clear what aspect of diabetes is the underlying cause for this increased risk, but one hypothesis centers on the elevated concentration of insulin typically seen in people with type II diabetes.

"In the early stages of the disease process, people become insulin resistant, meaning they must produce more and more insulin to regulate their blood sugar," Flood said. "Even after frank diabetes begins, insulin levels remain chronically elevated for extended periods before the pancreas can no longer supply the level of insulin the body demands. If the elevated insulin is the problem, then pre-diabetics, who are also hyper-insulinemic, should also be at increased risk (for developing colorectal cancer)."

To test that idea, Flood and his colleagues re-analyzed the data, this time including women who were likely prediabetic at the beginning of the follow-up period. These women were likely hyperinsulinemic at that stage. Surprisingly, the elevated risk, while still significant, had dropped slightly in comparison with that of known diabetics.

This suggests that either the pre-diabetic women had not had elevated insulin long enough or intensely enough to increase risk as they observed in the diabetic women, or alternatively, something other than or in addition to hyper-insulinemia could explain the significant, increased risk for colorectal cancer they observed in people with diabetes.

NCI-Approved Cancer Center, Cooperative Group Trials

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 Trial of CCL21 Gene Modified Dendritic Cells in Non-Small Cell Lung Cancer. University of California, Los Angeles, protocol 7888, Lee, Jay, phone 310-794-6566.

Phase I Dose-Escalation Study of Oral ABT-888 Plus Intravenous Irinotecan Administered in Patients with Advanced Solid Tumors. Barbara Ann Karmanos Cancer Institute, protocol 7977, LoRusso, Patricia Mucci, phone 313-576-8716.

Phase I Study of IV Doxorubicin Plus Intraperitoneal (IP) Paclitaxel and IV or IP Cisplatin in Endometrial Cancer Patients at High Risk for Peritoneal Failure. Gynecologic Oncology Group, protocol GOG-9920, McMeekin, Scott, phone 405-271-8707.

Phase I Study of MK-0752 in Pediatric Patients with Recurrent or Refractory CNS Malignancies. Pediatric Brain Consortium, protocol PBTC-024, Fouladi, Maryam, phone 901-495-2094.

Phase I/II

Phase I/II Study of the Poly(ADP-Ribose) Polymerase-1. New Approaches to Tumor Therapy Consortium, protocol NABTT-0703, Brain Blakeley, Jaishri O'Neill, phone 410-955-8837.

Neoadjuvant Androgen Depletion in Combination with Vorinostat Followed by Radical Prostatectomy for Localized Prostate Cancer: Total Androgen-Receptor Gene Expression Targeted Therapy. Sloan-Kettering Cancer Center, protocol 7864, Slovin, Susan, phone 646-422-4470.

Phase III

Randomized Phase III Double-Blind Placebo Controlled Trail of Memantine for Prevention of Cognitive Dysfunction in Patients Receiving Whole-Brain Radiotherapy. Radiation Therapy Oncology Group, protocol 0614, Curran, Walter, phone 215-955-6700.

Phase III, Randomized, Double-blind, Placebo-controlled Evaluation of Pregabalin for Alleviating Hot Flashes. North Central Cancer Treatment Group, protocol N07C1, Loprinzi, Charles, phone 507-284-1623.

Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy. Radiation Therapy Oncology Group, protocol RTOG-0534, Pollack, Alan, phone 215-728-2940.

Phase III Prospective Randomized Comparison of Depot Octreotide Plus Interferon Alpha Versus Depot Octreotide Plus Bevacizumab Advanced, Poor Prognosis Carcinoid Advanced, Poor Prognosis Carcinoid Patients. Southwest Oncology Group, protocol S0518, Yao, James, phone 713-792-2828.

Pilot

Safety and Efficacy Trial of the Anti-Viral and Anti-Tumor Activity of Velcade Combined with (R)ICE in Subjects with EBV and/or HHV-8 Positive Relapsed/Refractory AIDS-Associated Non-Hodgkin's Lymphoma. AIDS-Associated Malignancies Clinical Trials Consortium, protocol AMC-053, Reid, Erin, phone 858-822-6197.