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THE
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Cancer research news for clinicians

NSABP Breast Cancer Prevention Trial Reports Final Results On Tamoxifen

Researchers from the National Surgical Adjuvant Breast and Bowel Project who conducted the landmark Breast Cancer Prevention Trial report a seven-year and final update of the trial results in the Nov. 16 issue of JNCI.

In this final report, reductions in breast cancer incidence among participants taking tamoxifen were found to be very similar compared to those reported in 1998 when initial findings from the BCPT were released.

The conclusion is supported by the observation that the incidence rate of breast cancer was relatively constant through seven years of follow-up among women who received tamoxifen and by the fact that the rate remained

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Cancer Screening:

Ovarian Cancer Screening Finds Cancers, But Also Many False Positives, Study Says

Ovarian cancer screening methods such as transvaginal ultrasound and testing for a protein biomarker called CA-125, alone or in combination, can detect cancer, but also can produce many false-positive test results, causing needless surgery, according to the results of a study sponsored by the U.S. National Cancer Institute.

The preliminary results from the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial were published Nov. 15 in the American Journal of Obstetrics and Gynecology.

The findings are based on an analysis of the trial participants' initial screening tests. CA-125 and TVU have been considered as potential screening techniques, although studies to date have not shown that they can be effective and thus they are not currently recommended. The long-term objective of the PLCO Trial is to determine whether screening with TVU and/or CA-125 decreases ovarian cancer mortality in women ages 55 to 74.

Of the 28,816 healthy women who underwent the initial (baseline) screening, 1338 (4.7 percent) had an abnormal TVU and 402 (1.4 percent) had an abnormal CA-125 blood test. Thirty-four women (0.1 percent) had abnormal results in both screening tests. Among the women with abnormal test results, 29 tumors were detected, 20 of which were invasive cancers.

Women who had an abnormal test result in one or both screening tests underwent a variety of diagnostic procedures to determine whether cancer was present, including 570 women who underwent a surgical procedure as follow-up. Thus, 541 women underwent surgery but did not have cancer.

"Ovarian cancer is a disease that is often fatal, and both patients and

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BCPT: "A New Paradigm For Breast Cancer Prevention"

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stable for at least two years beyond the time that women stopped taking the drug.

The risks of stroke, deep-vein thrombosis, and cataracts—possible side-effects of tamoxifen treatment—were also similar to those reported previously.

"The BCPT should be viewed not only as the first study that demonstrated that breast cancer can be prevented, but also as a beginning from which a new paradigm for breast cancer prevention can evolve," said Bernard Fisher, first author of the initial and final reports, and principal investigator for the trial. "Cohorts of women at increased risk for breast cancer, who could derive a net benefit from receiving tamoxifen, have been clearly defined."

The BCPT was designed to see whether the drug tamoxifen could prevent breast cancer in women who were at an increased risk of developing the disease. Women in the study were randomly assigned to receive tamoxifen or a placebo, and neither participants nor their physicians were aware of the treatment assignment. Since 1998, BCPT participants have been followed by the NSABP, the Pittsburgh-based research network that conducted the trial with support from the U.S. National Cancer Institute.

When the initial results of the BCPT were first announced, researchers found a 49 percent reduction in invasive breast cancer incidence among participants at increased risk for the disease who took tamoxifen (Nolvadex, AstraZeneca Pharmaceuticals), a drug that had been used for over 20 years to treat breast cancer. The initial study results also showed a 45 percent reduction in non-invasive breast cancer incidence.

By 2005, after seven years of follow-up, investigators found that healthy women assigned to take tamoxifen developed 145 cases of invasive breast cancer compared to 250 cases in the women assigned to take placebo. This final analysis confirms that tamoxifen reduces the risk of invasive breast cancer in both pre- and post-menopausal women at increased risk for the disease, the investigators said.

Risk of pulmonary embolism was 11 percent lower than initially reported and risk of endometrial cancer was about 29 percent higher, but neither of these differences was statistically significant.

"The NCI is very pleased with the ultimate results of the BCPT, in part because there is proof of a benefit from tamoxifen beyond the time a woman is taking the pills," said Leslie Ford, associate director for NCI's Division of Cancer Prevention and co-author of the study. "We hope that other breast cancer prevention clinical trials, such as STAR, the Study of Tamoxifen and Raloxifene, help us identify drugs that maximize the benefits and minimize the side effects for women interested in reducing their risk of developing breast cancer."

Begun in April 1992, the BCPT also looked at whether taking tamoxifen decreased the number of heart attacks and reduced the number of certain common types of bone fractures in these women. There was almost no difference in the number of heart attacks between the tamoxifen and placebo group, but women in the tamoxifen group had fewer bone fractures of the hip, wrist, and spine (80 cases in the tamoxifen group vs. 116 cases in the placebo group) as reported in 2005.

Only women at increased risk of developing breast cancer participated in the study. Because the risk of breast cancer increases with age, women 60 years of age and older qualified to participate based on age alone. At age 60, about 17 of every 1,000 women are expected to develop breast cancer within five years. Women between the ages of 35 and 59, who demonstrated an increased risk of breast cancer equivalent to or greater than that of an average 60-year-old woman, were also eligible.

For information on NSABP clinical trials, go to http://www.nsabp.pitt.edu. For information about future breast cancer prevention trials, go to http://www.breastcancerprevention.com.

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Cancer Screening:

Decline In Breast Cancer Death Explained By Screening, Adjuvant Therapy, Study Finds

Early detection through screening mammography and improved adjuvant treatment have contributed almost equally to the substantial decrease in breast cancer death rates over the past 10 to 15 years, researchers conclude in an unprecedented effort to parse out the factors that have led to the decline.

The study, published in the Oct. 27 issue of the New England Journal of Medicine, was supported by the U.S. National Cancer Institute and conducted by seven research groups.

Researchers sought to end the longstanding controversy of whether screening mammography, better treatment or a combination of the two is responsible for improved breast cancer survival. The seven teams consisting of 43 investigators designed their own statistical models to determine the contribution of each method. These independent models used the same sources of data, some of which had not been mined before, but their approaches and assumptions differed.

The teams reached somewhat different conclusions, but were closest to each other in estimating how much the adjuvant therapies tamoxifen and chemotherapy reduced mortality in patients (12 percent to 21 percent, with a median of 19 percent). The range for screening mammography, however, was 7 percent to 23 percent (with a median of 15 percent), reflecting the greater uncertainty associated with estimating the benefit of screening.

Still, according to the models, the combination of screening and adjuvant therapy together reduced the breast cancer death rate by an estimated 25 percent to 38 percent, with a median of 30 percent. That explains the drop in breast cancer mortality from 1975 to 2000, according to the study's lead author, Donald Berry, chairman of the Department of Biostatistics and Applied Mathematics at M. D. Anderson Cancer Center.

"While we didn't agree with each other as to the percentages of benefit, all seven groups concluded that the decline in the rate of death from breast cancer is a combination of screening and therapy and not restricted to one or the other," he said. "Screening would have no benefit if not followed by treatment, including surgery, and treatment has the potential to be more effective if cancer is detected at earlier stages by screening."

Berry stresses that the differences in conclusions reflect uncertainties in the interpretation of available information and differing modeling approaches, rather than contradictions among the models. "These are seven top modeling groups applying their efforts to the best data that we have available in this country," he said.

The survival benefits offered by screening and adjuvant therapy both may be lower than researchers had expected, Berry said. "Some people think the benefit of screening is huge, and others say that the reduction in death rates is due primarily to adjuvant therapy," he said. "No one has known for sure, and although we still don't know for sure, this is the best set of analyses that is possible given the available information."

The study was undertaken by the Cancer Intervention and Surveillance Modeling Network (CISNET), a consortium of investigators sponsored by the NCI whose purpose is to measure the effect of cancer-control interventions on the incidence of and risk of death from cancer in the general population. The seven breast cancer teams involved in this study are from Dana-Farber Cancer Institute; Erasmus University Medical Center in Rotterdam, the Netherlands; Georgetown University; M. D. Anderson Cancer Center; Stanford University; the University of Rochester; and the University of Wisconsin-Madison.

In 1975, the rate of death from breast cancer among women 30 to 79 years of age, adjusted for age to the 2000 population, was 48.3 deaths per 100,000 women. By 1990, the rate had increased slightly to 49.7 per 100,000, but then fell to 38.0 per 100,000 by 2000, a decrease of 24 percent from 1990.

The two major changes in breast oncology over that time have been the advent of screening mammography (which 70 percent of women over age 40 received in 2000) and the use of adjuvant therapies—chemotherapy and hormone therapy used in conjunction with primary treatment by surgery and/or radiation. But because each of these factors gained in popularity and use at about the same time, it is not a simple matter to separate out the relative contribution of each to improved survival, Berry said.

To find out, the CISNET groups used data that reflected "real life" use of screening and adjuvant therapy, including some population databases that had not been tapped before for this purpose. Their analysis relied on the incidence of breast cancer as reported by the Surveillance, Epidemiology, and End Results program and the rate of death from breast cancer as reported by the National Center for Health Statistics, as well as additional databases concerning uses of screening and treatment and their efficacy in the population.

The models reached somewhat different

estimates. Dana-Farber's model found that screening mammography accounted for 65 percent of the reduced breast cancer death rate (with 35 percent due to use of chemotherapy and tamoxifen) while the M. D. Anderson model reached the opposite conclusion—that 65 percent of the mortality benefit is due to adjuvant chemotherapy and 35 percent is due to screening.

Berry has studied mammography and has focused on its downside. The researchers who conducted the study are comfortable with the level of disagreement concerning their point estimates and with the level of uncertainty reflected in their overall conclusions, he said. In his opinion, "the evidence makes clear that the benefit of screening on breast cancer mortality is very likely while the benefit of providing adjuvant therapy is certain." He continues to feel strongly that women should be informed of the risks of screening as well as the benefits, and says he is "happy to have helped further quantify the latter."

The models now in place can be used to answer a number of questions related to screening and treatment, Berry said. "They provide a way for assessing the benefits of screening and treatment strategies different from the ones that were actually in place over the time period of the study," he said. "For example, our models can address what the effect on mortality would be if all women in particular age groups were to be screened at regular intervals. And it allows for addressing the impact on overall mortality if effective therapies were made available to particular types of patients with breast cancer."

In this way, the models may "help determine what strategies for delivering medical care are best for patients," Berry said. "And that is necessary, since our efforts, taken as a whole, haven't come close to eliminating breast cancer mortality."

Ovarian Cancer Screening False-Postive Rate High

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physicians are anxious to find ways to detect it at an earlier, more curable stage," said first author on the study, Saundra Buys, of University of Utah. "However, the results from the initial year of screening show that TVU and CA-125 cannot currently be recommended for widespread use in the general population. Future results from the additional PLCO screenings and subsequent follow-up will be needed before a final assessment of this screening strategy can be made."

Enrollment in the PLCO study began in 1993 and ended in 2001. When they enrolled in the study, women in the intervention arm underwent baseline ovarian cancer screening with CA-125 and TVU and received additional annual screenings and follow-up. Women in the control arm of the study were not screened but were observed over time.

The results published in this report reflect analysis of the initial baseline screenings for women enrolled between 1993 and 2001. The results of subsequent years screening with TVU and CA-125 are not yet available, and it is these additional results that will ultimately determine whether this screening strategy is effective in reducing mortality from ovarian cancer. These results will not be available for several years.

At the time of the baseline examination, both TVU and CA-125 had low predictive values—a measure of how likely a person with a positive test result is to have the disease of interest—when used to screen healthy women for ovarian cancer. Many investigators feel that an acceptable predictive value for an ovarian cancer screening test is around 10 percent. The predictive values of these screening tests were 3.7 percent for an abnormal CA-125 test, 1 percent for an abnormal TVU, and 23.5 percent if both tests were abnormal. Although having an abnormality in both tests had a fairly high predictive value, only 9 of the 29 tumors (31 percent) were associated with abnormalities in both tests.

The PLCO is scheduled to collect data until 2008.

ASCO Supports CT Scans For Colorectal Screening

A colorectal cancer surveillance guideline panel of the American Society of Clinical Oncology recommended annual computerized tomography scan in high-risk patients to determine if the cancer has spread to the lungs or liver.

These scans are recommended for the first three years after treatment for patients who have a higher risk of recurrence and who would be good candidates for surgical removal of a secondary tumor.

High-risk patients have lymph node involvement at surgery or other poor prognostic factors like lymphatic vessel invasion. A CT scan of the pelvis is also recommended for rectal cancer patients who have a high risk of recurrence, and who have not had radiation therapy.

"In the past, ASCO did not recommend CT scan for regular follow-up care because the published studies were not convincing that anything other than a

carcinoembryonic antigen [CEA] blood test was useful," said Christopher Desch, lead author of the guideline and research director at the Virginia Cancer Institute. "However, when the study data were pooled, results emerged suggesting annual CT scanning may save lives by finding patients with resectable metastases.

"These recommendations do not apply to patients with stage I or most patients with stage II colorectal cancer," Desch said. "As a rule of thumb, the recurrence rate should be close to 50% before these tests are ordered."

The CT scan recommendation was the most significant change in the update to the colorectal cancer surveillance guidelines.

ASCO also recommends regular doctor visits as a part of follow-up care. Since most colorectal cancer recurrences develop within three years after surgery, doctor visits are recommended every three to six months for the first three years, every six months during years four and five, and as often the doctor and patient decide after year five.

Regularly scheduled visits help increase the likelihood of finding a treatable recurrence and also provide patients with reassurance about their situation. Regular visits also give patients and doctors a forum to discuss new findings for follow-up care or risk of other cancers.

"Because of new technology, such as Web-based prediction tools that help doctors estimate the risk of recurrence, it is even more beneficial for patients and doctors to schedule regular visits and evaluate cancer risk," Desch said.

The new guideline also recommends that patients with stage II or III colorectal cancer undergo a CEA blood test every three months, for at least three years after diagnosis, once adjuvant therapy is finished. High levels of CEA in the blood may indicate that a cancer has spread to other parts of the body.

While a CEA test is recommended, other blood tests, such as a complete blood count (CBC) test, liver function tests, or fecal occult blood test, are not recommended by ASCO for follow-up care because there is not enough scientific evidence to support a recommendation.

Following surgery, a colonoscopy, is recommended at three years and then, if the findings are normal, every five years thereafter. Some patients, such as those with high-risk hereditary colorectal cancer syndromes, may require more frequent colonoscopy screening.

Lastly, a flexible proctosigmoidoscopy is recommended every six months for five years for patients with stage II or III rectal cancer who did not receive radiation therapy. During a proctosigmoidoscopy, a sigmoidoscope is inserted into the rectum and lower colon to check for polyps, cancer, and other abnormalities.

The updated guideline was published online Oct. 31, in the Journal of Clinical Oncology.

For a copy of the guideline, visit www.asco.org/guidelines. A patient guide is available on ASCO's patient website at www.plwc.org.

CT Scan Can Spare Surgery In Head And Neck Cancer

Some patients with head and neck cancer can be safely spared the risk and expense of surgery by undergoing a CT scan to predict whether the disease is in check after radiation therapy, according to study findings presented last month at the annual meeting of the American Society for Therapeutic Radiology and Oncology.

Researchers at the University of Florida Shands Cancer Center have identified criteria doctors can use to evaluate CT scans four weeks after patients undergo initial treatment. If these criteria are met, there is a 94 percent likelihood a patient's lymph nodes are cancer free, said Stanley Liauw, a resident in radiation oncology. Using a CT scan was found to be much more accurate than relying on a physical exam to assess response to treatment.

Radiation therapy is commonly used to treat patients who develop advanced head and neck cancer. After radiation therapy, doctors often operate to remove affected lymph nodes. But UF physicians say in some cases surgery is unnecessary, and can increase recovery time, lead to infection and possibly compromise a patient's quality of life.

The current study builds on previous research involving 95 head and neck cancer patients. In two-thirds of the patients who underwent surgery after radiotherapy, the removed lymph nodes turned out to be cancer free, noted UF radiologist Anthony Mancuso, who collaborated with UF radiation oncologists Robert Amdur, Christopher Morris, and William Mendenhall.

By comparing nodes visualized on a CT scan with the same nodes after they were removed, the researchers developed criteria doctors could use to examine nodes using a non-invasive CT scan to identify whether the disease was knocked out. Nodes deemed to be clear of cancer were 1.5 centimeters or smaller and had borders that were sharply defined on the CT scan.

In the current study, UF researchers examined the

medical records of 549 patients who were treated with radiotherapy at UF for advanced head and neck cancer between 1990 and 2002; 341 patients later underwent surgery to remove lymph nodes. UF doctors, basing their treatment on the results of the previous research, did not remove lymph nodes in patients who met the CT scan criteria.

Results confirmed that a CT scan could be used to reliably predict whether the lymph nodes would be negative for cancer.

A simpler method of CT interpretation (using lymph node size and the presence of an abnormal appearance within the lymph node) predicted, with a 94 percent accuracy, when a patient was cancer free. In 33 patients who were spared neck dissection on the basis of their post-treatment CT scan, only one suffered a recurrence of the disease in the lymph nodes. That patient was then scheduled for surgery, and the involved nodes were successfully removed. The patient recovered.

A newer imaging technology, the PET scan, cannot give an accurate reading of the nodes until two to three months after radiation therapy, making it impossible to surgically intervene in a timely manner, said Mancuso, a co-investigator.

"There is no other alternative method that is effective within the six-week decision-making window," Mancuso said.

Suresh Mukherji, chief of neuroradiology at the University of Michigan, said the data was promising and could lead to improvements in patient treatment.

"So far this is a single institute study. We need to have multiple institutes adopt this and see if results are similar over the long term," Mukherji said.

Breast Cancer:
Herceptin Lowers Recurrence In Early Breast Cancer

The targeted drug trastuzumab, or Herceptin, previously shown to prolong survival in advanced breast cancer, dramatically reduced the chances of recurrence in patients with early-stage disease when given for one year following standard chemotherapy.

These are the encouraging findings in an interim report from HERA, an ongoing large, international clinical trial of Herceptin, being published in the New England Journal of Medicine on Oct. 19.

The analysis was led by Richard Gelber, of Dana-Farber Cancer Institute, who led the statistical analysis for the HERA trial, which is one of the largest breast cancer trials to date.

The study includes more than 5,000 patients in 39 countries.

Women whose tumors were HER2-positive—overexpressing a protein associated with more aggressive cancer and poorer outcomes—had approximately a 50 percent lower risk of disease recurrence. This translated into an 8 percent improvement in the number of women who were free of disease two years after beginning the treatment.

"This is probably the biggest evidence of a treatment effect ever seen in oncology," said Gelber.

"Now we have made dramatic progress for patients with HER2-positive breast tumors, who now have a much lower risk of recurrence and better chance of survival because of trastuzumab," Harold Burstein, of Dana-Farber, wrote in a commentary published with the report.

The interim data were released last May at the annual meeting of the American Society of Clinical Oncology, prompting standing ovations from cancer specialist attending the conference.

Herceptin is a monoclonal antibody-based drug developed specifically to block the activity of the HER2 protein, a growth factor receptor that is overexpressed on cancer cells of an estimated 20 to 30 percent of breast cancer patients. HER2-positive tumors, which can be identified with a test when the breast cancer diagnosis is made, are generally more aggressive and prone to spreading, and are resistant to many chemotherapy agents.

The HERA trial, sponsored by Roche, the manufacturer of Herceptin, and carried out by the Breast International Group (BIG), a federation of international breast cancer clinical trial cooperative groups, began enrolling patients in 2001.

The aim is to determine whether Herceptin treatment improves outcomes in early HER2-positive breast cancer when added to standard chemotherapy. More than 5,000 women had surgery and various types of chemotherapy drugs before entering the trial. About two-thirds had cancer that had spread to the underarm lymph nodes.

One group of 1,694 patients received Herceptin every three weeks for one year; another 1,694 received it for two years. No Herceptin was administered to the third group of 1,693 patients.

Recurrences in HER2-positive breast cancer tend to happen in the first year or two. When the statisticians took their first look at the data after one year, the benefits in the Herceptin group were already apparent.

"The differences showed up so quickly that the Data Monitoring Committee felt that data had to be released, even though we don't know the long term effects and the long term side effects," said Gelber.

There were 220 recurrences in the group that did not receive Herceptin, compared with 127 in the group treated for one year with Herceptin.

The group receiving the drug had a significant improvement in disease-free survival of 8.4 percent at two years. Disease-free survival is the length of time after treatment during which patients show no signs of the disease.

Overall survival in the groups did not differ by a statistically significant amount, but that could change as the study continues, the researchers say. The study is planned to run through 2008.

The researchers were gratified to discover that only 0.5 percent of the patients receiving Herceptin had serious cardiac side effects. It was a concern because in previous trials combining chemotherapy with Herceptin the rate had been significantly higher.

The scientists said that the lower incidence of cardiac side effects in the HERA Trial may be related to the facts that Herceptin was administered after chemotherapy treatment had been completed, instead of simultaneously, and that patients with insufficient cardiac function after chemotherapy were not included.

The journal also published results of two other Herceptin trials among North American patients, with similar findings of effectiveness.

Cancer Care:
Improvements Still Needed To Reduce Chemo Errors

In one of the first studies to examine chemotherapy errors in ambulatory care for cancer patients, researchers at Dana-Farber Cancer Institute and Brigham and Women's Hospital found that about three percent of chemotherapy orders in three outpatient infusion clinics studied contained mistakes.

Most of the errors were intercepted by nurses and pharmacists before reaching patients, and none were life-threatening or caused patient harm.

However, the results show that room for improvement exists even in hospitals with strong error-prevention programs, the authors said.

The research, reported in the journal Cancer, was made possible by Dana-Farber and BWH leaders' decision to share drug-order and patient-safety records with investigators. The findings of the study have prompted both hospitals to make changes in automated drug order-entry system to further lessen the chance of mistakes.

"Our results show that while safeguards such as computerized order-entry systems used at both Dana-Farber and Brigham and Women's significantly reduce drug-order errors, additional improvements are still possible, and necessary," said the study's co-lead author, Tejal Gandhi, of BWH.

"DFCI's leadership supported the in-depth review of all medication orders to gain information about potential system defects," said co-lead author Sylvia Bartel, of DFCI. "The goal was to utilize the results of the study to make system improvements and ensure a safe medication process for our patients."

Previous studies have estimated that about five percent of drug orders for hospitalized patients have errors, but much less scientific attention has been given to the prevalence of such mistakes in outpatient settings.

In the study, the researchers reviewed more than 10,000 medication orders from Dana-Farber's adult and pediatric ambulatory oncology infusion clinics, which used a computerized or paper medication-ordering system.

Using a strict definition of error, they found that three percent of the orders contained errors, one-third of which were deemed serious.

Rating the errors by severity, researchers determined that 82 percent of the errors in adults and 60 percent in children had potential for harm to patients.

Pharmacists and nurses caught 45 percent of the potentially harmful errors before they reached patients, and none of the errors actually caused patient harm.

In the adult clinics, which used a computer-aided ordering system, and the pediatric clinic, where a paper-based ordering system was in place, the most frequent errors involved omitted or incorrect dosages and failure to discontinue orders.

To reduce the chances of future medication order errors, officials at DFCI have instituted several changes.

In the pediatric clinic, orders are now placed via computer. In the adult clinics, physicians now use a more sophisticated computer application with more of the drug-ordering information embedded within it.

For medications that are usually given in tandem, the program now requires physicians to order both at the same time.

The study was supported by a grant from the Harvard Risk Management Foundation.

Multiple Myeloma:

T-Cell Vaccines Cut Time To Protective Immunity

Patients with multiple myeloma suffer from a malignant proliferation of plasma cells in their bone marrow. The standard treatment is high-dose chemotherapy and transplantation of one's own blood-producing adult stem cells; however, this wipes out the mature immune-system cells of patients, leaving them vulnerable to infection.

A treatment currently approved is to vaccinate myeloma patients against pneumococcus a year after their transplantation. But why wait a year, wondered researchers at the University of Pennsylvania School of Medicine?

Their investigation revealed that protective levels of immunity against pneumococcus could be obtained in patients who were given the prophylactic bacterial vaccine in addition to a new autologous T-cell-based vaccine only two weeks after transplantation. Protection developed in the patients within a month after the transplantation. The results of their clinical trial was published last month in Nature Medicine.

"We found that we can rapidly rebuild the patients' immunity after chemotherapy and stem-cell transplant," said Carl June, director of translational research at Penn's Abramson Cancer Center.

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 Pharmacokinetic and Pharmacodynamic Study of Temsirolimus in Patients with Advanced Malignancies and Normal and Impaired Liver Function: An NCI Organ Dysfunction Working Group Study. Cancer Therapy and Research Center, protocol 6813, Takimoto, Chris, phone 210-562-1725.

Phase I Study of Vorinostat in Combination with Decitabine in Patients with Advanced Solid Tumors, Patients with Advanced Solid Tumors, Relapsed or Refractory Non-Hodgkin's Lymphoma, Acute Myeloid Leukemia, Acute Lymohocytic Leukemia, or Chronic Myelogenous Leukemia in Blast Crisis. Princess Margaret Hospital Phase II Consortium, protocol 6869, Yee, Karen, phone 416 946 2911.

Phase I/II

Phase I-II Trial of Fenretinide(4-HPR) + Rituximab in Patients with B-cell Lymphoma. University of Washington Medical Center, protocol 6957, Gopal, Ajay, phone 206-288-2037.

Phase II

Phase II Study of BAY 43-9006 in Chemosensitive Relapsed Aggressive Non-Hodgkin's Lymphomas. University of Maryland Greenebaum Cancer Center, protocol 7058, Heyman, Meyer, phone 410-328-2594.

Phase II Trial of PS-341 in Combination with Paclitaxel and Carboplatin for the Treatment of Metastatic Melanoma. Mayo Clinic Rochester, protocol 7216, Croghan, Gary, phone 507-284-3902.

Limited Access Phase II Trial of Weekly Topotecan Paclitaxel and Cisplatin in the treatment of Advanced, Persistent, or Recurrent Carcinoma of the Cervix. Gynecologic Oncology Group, protocol GOG-0076EE, Long, Harry, phone 507-284-4320.

Phase II Trial of O6-Benzylguanine and Temozolomide in Pediatric Patients with Recurrent or Progressive High-Grade Gliomas and Recurrent or Progressive Brainstem Tumors. Pediatric Brain Tumor Consortium, protocol PBTC-015, Warren, Katherine, phone 301-402-6298.

Phase II Trial of Pemetrexed in Patients with Selected Stage IIIB and IV Bronchioloalveolar Carcinoma. Southwest Oncology Group, protocol S0526, Davies, Angela, phone 916-734-3772.

Phase III

Phase III, Randomized Trial of Weekly Cisplatin and Radiation Versus Cisplatin Group and Tirapazamine and Radiation in Stage IB2, IIA, IIB, IIIB and IVA Cervical Carcinoma Limited to the Pelvis. Gynecologic Oncology Group, protocol GOG-0219, DiSilvestro, Paul, phone 401-453-7520.

Phase III Clinical Trial Comparing Oxaliplatin, Capecitabine and Hepatic Arterial Infusion of Floxuridine to Oxaliplatin and Capecitabine in Patients with Resected or Ablated Liver Metastases from Colorectal Cancer. National Surgical Adjuvant Breast and Bowel Project, protocol NSABP-C-09, Wagman, Lawrence, phone 626-359-8111, x63058.

Other

Identifying Genomic Predictors of Recurrence after Adjuvant Chemotherapy. Eastern Cooperative Oncology Group, protocol 7613, Sparano, Joseph, phone 718-904-2555.

A Notch-Signaling Pathway Inhibitor in Patients with T-cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL)

An investigational study for children, adolescents and adults with relapsed and refractory T-cell acute lymphoblastic leukemia/lymphoma is now accruing patients at various centers around the country.

This study's goal is to evaluate the safety and tolerability of a Notch inhibitor as a rational molecular therapeutic target in T-ALL, potentially uncovering a novel treatment for these cancer patients.

Eligibility criteria and treatment schema for the study include:

Notch-Signaling Pathway Inhibitor in Patients with T-ALL	
Eligibility Criteria	Patient must be = 12 months with a diagnosis of T-cell acute lymphoblastic leukemia/lymphoma AND must also have: • Relapsed T-ALL • T-ALL refractory to standard therapy • Not be a candidate for myelosuppressive chemotherapy due to age or comorbid disease ECOG performance status =2 for patients >16 years of age OR Lanksy performance level >50 for patients 12 months to =16 years of age Fully recovered from any chemotherapy and >2 weeks from radiotherapy, immunotherapy, or systemic steroid therapy with the exception of hydroxyurea or intrathecal therapy Patient must be >2 months following bone marrow or peripheral blood stem cell transplantation No treatment with any investigational therapy during the preceding 30 days No active or uncontrolled infection
Treatment Plan	Open label and non-randomized, this study is conducted in two parts. Part I is an accelerated dose escalation to determine the maximum tolerated dose (MTD), and Part II is a cohort expansion at or below the MTD. MK-0752 will be administered orally. Plasma concentrations will be measured at defined time intervals.

For information regarding centers currently open for enrollment, please contact 1-888-577-8839.