Vol. 31 No. 1
January 2008

THE
CLINICAL CANCER LETTER
Cancer research news for clinicians

Prostate Cancer:

Early, Short Course Of Hormonal Therapy May Allow Patients To Live Longer

Researchers report that four months of hormonal therapy before and with standard external beam radiation therapy slowed cancer growth by as much as eight years—especially the development of bone metastases—and increased survival in older men with potentially aggressive prostate cancer.

This "neoadjuvant" hormonal therapy may allow men most at risk of developing bone metastases avoid long-term hormonal therapy later on. Also, the short-term hormonal therapy did not increase the risk of cardiovascular

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Breast Cancer:

High-Dose Chemo, Stem Cell Transplant No Benefit For Node+ Breast Cancer

High-dose chemotherapy and autologous stem cell transplantation, the controversial, arduous, yet once-popular combination treatment that fell out of favor as a therapy for breast cancer, has proven not to be beneficial as an adjuvant therapy for women with node-positive disease, according to an analysis by researchers at University of Texas M. D. Anderson Cancer Center.

In a review of 15 randomized high-dose chemotherapy studies conducted around the world between 1988 and 2002, the investigators from M. D. Anderson, in collaboration with the European Blood and Marrow Transplant Group, report that while there was a slight benefit on relapse-free survival, there was no benefit to overall survival.

Donald Berry, professor and head of the Division of Quantitative Sciences, presented the findings at the San Antonio Breast Cancer Symposium last month.

"Of all cancers, breast cancer is one of the most sensitive to treatment, resulting in a dramatic mortality decrease in the U.S. in recent years," Berry said. "Frequently, in recent breast cancer history, when we have run studies of adjuvant therapy for node-positive breast cancer, the findings have shown that an innovation indeed delays recurrence and prolongs survival. For example, we've shown that increasing doses of the chemotherapy regimen FAC within the standard dose range improves overall survival and disease-free survival. We've shown the same for the addition of paclitaxel. We've also proved that dose density, in terms of delivery every two weeks versus every three weeks, improves overall survival.

"All of these studies suggest the more you do, the better. It's clear to

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Early Hormonal Therapy Delays Bone Metastasis

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disease, a potential side effect of long-term hormonal therapy. The study was published online earlier this month in the Journal of Clinical Oncology.

Hormonal therapy, called androgen deprivation therapy (ADT), lowers levels of cancer-fueling testosterone in the blood. It is an important treatment option for men with prostate cancer that continues to progress despite initial treatment with surgery, radiation therapy, or chemotherapy, but has been associated with side effects such as bone loss, osteoporosis, depression and an increase in cardiovascular risk factors (including blood lipids, abdominal obesity and a syndrome associated with diabetes).

"This study demonstrates that the benefits of short-term hormonal therapy for men receiving radiation therapy for prostate cancer far outweigh the risks," said lead author Mack Roach III, professor and chairman of radiation oncology and professor of urology at the University of California, San Francisco. "While four months of hormonal therapy isn't enough to cause significant side effects, we found that it can delay the development of bone metastasis by as many as eight years, which is very significant."

Starting in 1987, Radiation Therapy Oncology Group researchers studied 224 men with high-risk prostate cancer who received ADT (goserelin and flutamide) before and concurrent with external beam radiation therapy, and 232 men with the disease who received radiation therapy alone. After 13 years of follow up, they found better 10-year disease-specific death rates (the rate of death from prostate cancer) for men who received ADT plus radiation (23 percent versus 36 percent of the radiation-only group), disease metastasis rates (35 percent versus 47 percent), disease-free survival (the percentage of men free of cancer at 10 years; 11 percent versus 3 percent) and biochemical failure rates (a rise in PSA levels; 65 percent versus 80 percent).

Among men who received neoadjuvant hormonal therapy, there was up to an eight-year delay in the time it took 40 percent of patients to develop bone metastases compared with men receiving radiation alone. Men who develop bone metastases often require long-term hormonal therapy, which can increase their risk for side effects.

"So by taking a little bit of hormonal therapy early, patients may avoid having to take a lot of it later," Roach said.

Fatal cardiac events occurred in 12 percent of patients in the ADT group compared with 9 percent of the radiation-only group—a difference that was not statistically significant.

The Clinical Cancer Letter

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PO Box 40724, Nashville TN 37204-0724

THE CLINICAL CANCER LETTER (ISSN 164-985X). Published monthly, subscription $125 per year, by The Cancer Letter Inc.

Breast Cancer:

No Benefit Seen In Analysis Of HDC/Stem Cell Transplant

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me that delivering more chemotherapy must benefit some patients. Yet, there is a limit and we seem to have reached a plateau."

Adjusting for demographics, clinical characteristics, intensity of therapy, estrogen receptor status, Berry thought the study would show a statistical significance in overall survival.

"At a minimum, I thought we would have a chance to identify subsets of patients that would benefit and, with 6,200 patients randomized in the 15 trials, that we would be able to confirm our findings. The fact that we did not identify such subsets in no way lessens the value of our study. It is the definitive study for high-dose breast cancer in the adjuvant setting," Berry said.

To appreciate the importance of the study itself and its findings one must understand the nature of the therapy and its conflicting history.

High-dose chemotherapy can be arduous for the patient: it includes administering very high doses of chemotherapy followed by bone marrow or stem cell

transplantation of the patient's own blood stem cells that are collected prior to receiving chemotherapy. The autologous transplant rebuilds the bone marrow, which was effected by the intense chemotherapy, said Naoto Ueno, associate professor in M. D. Anderson's Departments of Stem Cell Transplantation and Cellular Therapy and Breast Medical Oncology. While it has become far more tolerable, in the past, the therapy was often debilitating and was associated with a number of serious side effects, including infection, nausea, vomiting, and extreme weakness, sometimes resulting in death from the treatment alone.

"The 1980s and early 1990s represented a period in breast cancer history where more was better in terms of treatment," said Ueno, an author on the study.

Despite its side effects, a few small studies emerged in the early 1990s suggesting that the treatment was beneficial for women with high-risk breast cancer, those with at least 10 positive axillary lymph nodes. Yet, these studies were not randomized, the gold standard for testing a therapy, explains Berry. Rather they compared one database to another.

Regardless, breast cancer patients and advocates began demanding the treatment and that the therapy, which averages $100,000, be covered by insurance. According to Berry, approximately 20,000 women with breast cancer in the U.S. received high-dose chemotherapy.

Most randomized trials of the therapy were begun in the 1990s and did not confirm earlier positive findings. Rather, most of these trials showed little or no benefit for women with breast cancer. The therapy's stature became even more confusing when data from a large randomized positive trial, presented on the plenary session of the 1999 American Society of Clinical Oncology, was later found to be falsified.

"It was important to do this study so it could be determined if there is any evidence of a benefit to patients, or if there is any subset of patients that benefited from the therapy," Berry said.

For their analysis, the investigators built an expansive database and looked at all 15 trials conducted in the world. More than 6,200 women were enrolled in the studies and were randomized to receive either high-dose chemotherapy (3,118 patients) or additional doses of the standard chemotherapy (3,092 patients).

The median patient follow-up was seven years and the mean age of the women enrolled in the trials was 45. Of the women, hormone receptor status was positive in 55%, negative in 28% and not available in 17%. The decrease in the rate of breast cancer relapse due to higher dose chemotherapy was 13%, which was statistically significant. However, the benefit did not translate into survival. The decrease in mortality rate was 6%.

After adjusting for age, trial, hormone status, tamoxifen use and the number of positive lymph nodes, the high-dose regimen slightly improved relapse-free survival by about eight months. However, there was no survival benefit for women who received high-dose chemotherapy.

In the analysis, it was important to focus on the role of dose intensity, Berry said. "In terms of just how high of a dose the chemotherapy was, some trials used very high doses, while others used more moderated doses, but still high enough to require stem cell support."

Regarding dose intensity, if a study had a big difference in dose intensity between the high and standard dose that was allowed to play a greater role in the investigators' conclusions. If a study had a smaller higher dose or if the standard dose was quite high, then it would not count as much in terms of the comparison between the high- and the standard-dose groups, said Berry.

"Still, even adjusting for trial and dose differences, we were not able to tease out more than a marginal benefit for greater dose intensity."

The catch is that the chemotherapies under study are known to be effective. Therefore there has to be some sort of dose effect.

"What we are learning is that the doses used in standard chemotherapy regimens for advanced breast cancer have reached a plateau and that increasing beyond that dose is not delivering a greater benefit," said Berry. "It is likely that there are patients who respond to a specific chemotherapy type. Once you give enough of that chemotherapy to benefit those patients, there's no advantage from additional treatment. You are aiding those that were destined to benefit with moderate doses. The remainder of the patients have tumors that are not sensitive to the chemotherapy being considered and would not benefit no matter how much you give them."

Xeloda, Taxotere, Herceptin Combination May Benefit Invasive Breast Cancer

Interim results of the Phase II XeNA (Xeloda in NeoAdjuvant) trial suggest that the combination of oral Xeloda (capecitabine) and Taxotere (docetaxel), with the addition of Herceptin (trastuzumab) in HER2-

positive patients, may be an active and well-tolerated neoadjuvant (pre-surgical) treatment option for women with invasive breast cancer. These data were presented at the San Antonio Breast Cancer Symposium.

In the multi-center, open-label trial designed to investigate the activity of a short non-anthracycline-based preoperative treatment for early breast cancer in both HER2-negative and HER2-positive patients, promising results were achieved after only four cycles of pre-surgical treatment as compared to the standard eight cycles. The majority of the 156 patients responded to the Xeloda-based therapy regardless of HER2 status, and both patient groups experienced a clinically significant reduction in tumor size.

"These early XeNA trial results highlight the potential of the Xeloda/Taxotere combination, with Herceptin for HER2-positive patients, to provide an effective and safe treatment option in a shorter period of time before surgery among patients with invasive breast cancer," said Debu Tripathy, lead investigator of the XeNA trial and professor of medicine and director of the Komen/UT Southwestern Breast Cancer Research Program at the University of Texas Southwestern Medical Center at Dallas. "While these findings warrant additional studies, the real-world impact of the reduction in tumor size could translate into the difference between a lumpectomy instead of a more drastic mastectomy."

In the interim analysis, following four treatment cycles, the three-drug combination in HER2-positive patients resulted in a 73 percent clinical response rate (complete and partial response) and a 50 percent pathologic response (pathologic complete response, which is the absence of histological evidence of cancer cells in the tissue specimen, plus near pathological complete response, which is less than or equal to 5 millimeters of residual cancer).

Also, HER2-negative patients experienced a clinical response rate of 76 percent and 15 percent pathological response with the combination of solely Xeloda and Taxotere. In patients with HER2-negative tumors, a decrease from 6.1 to 2.8 centimeters was observed; in HER2-positive patients, the reduction was from 5.6 to 1.6 centimeters.

This multi-center, open-label XeNA trial enrolled 157 (156 evaluable) patients with newly-diagnosed invasive breast cancer (planned sample size 122 HER2-negative; 34 HER2-positive) and was designed to investigate the activity of a short non-anthracycline-based preoperative treatment for early breast cancer. Efficacy results for 134 patients as well as toxicity data for the total evaluable population (156 patients) were included in this interim analysis.

The primary endpoint was the rate of pathological complete response rate (pCR) plus near pCR in the affected breast after preoperative administration of Xeloda and Taxotere for HER2-negative patients and in combination with Herceptin for HER2-positive patients. Secondary endpoints included safety profile; quality of life; local recurrence; disease-free survival; distant disease-free survival; and overall survival.

Other secondary endpoints included pCR in sentinel and axillary, or underarm, lymph nodes; clinical response rate; ability of blood and tissue markers; genomic profiling of the tumors; circulating tumor cells for HER2-neu positive patients; and p53 gene mutations to predict short-term clinical and pathological responses.

Study participants were limited to female outpatients, aged 18 and older, who were diagnosed with HER2-negative or HER2-positive breast cancer, with no evidence of metastatic disease except ipsilateral axillary lymph nodes, or axillary lymph nodes found on the same side of the body, and no prior history of treatment.

Patients received four three-week cycles of the treatment regimen. HER2-negative patients received Xeloda 825 mg/m2 twice a day for 14 days with seven days off, and also received Taxotere 75 mg/m2 IV on the first day. HER2-positive patients were on the same regimen, but also received Herceptin each week with a loading dose of 4 mg/kg for 90 minutes followed by 2 mg/kg for 30 minutes for a total of 12 weeks before definitive surgery.

The most frequent adverse events (AEs) were hematologic toxicities and hand-foot syndrome. Five HER2-neu negative patients and one HER2-positive patient experienced progression before surgery. There were no treatment-related deaths prior to surgery, nor were there clinical or subclinical cardiac events.

Longterm Followup Finds Taxotere Improves Survival

Results presented at the 30th annual San Antonio Breast Cancer Symposium showed that for women with early stage breast cancer who have had surgery, treatment with the investigational chemotherapy combination of Taxotere (docetaxel) and cyclophosphamide significantly improved overall survival compared to standard chemotherapy.

The presentation reports results with a median follow-up of seven years and has been updated since

the last report was published with 5.5 years median follow-up. This latest report has also been updated from the abstract submitted to SABCS 2007.

In the updated analysis, overall survival at seven years was statistically higher among women treated with Taxotere® and cyclophosphamide (TC) versus those treated with doxorubicin and cyclophosphamide (AC): 87% versus 82% (HR: 0.69, [95% CI, 0.50, 0.97]). The 31% reduction in the risk of death was statistically significant (p=0.032). At seven years, the disease-free survival (DFS) was also statistically greater among women treated with TC than those treated with AC: 81% versus 75% (HR: 0.74, [95% CI, 0.56, 0.98]). The 26% reduction in the risk of cancer recurrence among women treated with TC was statistically significant (p=0.033). The disease-free survival benefit seen in the elderly patients (aged 65 years or older; 31% risk reduction of recurrence) is consistent with that in the overall patient population.

Principal investigator Stephen Jones, medical director and co-chair, breast cancer research committee of US Oncology, helped develop the regimen combining the anthracycline doxorubicin with cyclophosphamide, which became a foundation of breast cancer chemotherapy for more than 30 years.

"The investigational Taxotere combination significantly increased the percentage of women living with no signs of cancer at seven years, as compared to the anthracycline combination," Jones said.

USO Adjuvant Trial 9735 was designed primarily to evaluate disease-free survival among women with node-positive and node-negative early breast cancer. Node-positive indicates that the cancer has spread to the lymph nodes under the arm, while node-negative breast cancer means that the lymph nodes are clear of cancer.

Secondary endpoints included overall survival and safety. The investigators also explored the efficacy and safety of the treatments based on the age of patients and the biologic characteristics of their tumors.

All patients taking part in the study had received surgery for stage I-III invasive breast cancer, meaning that the cancer was either localized to the breast or had spread to the lymph nodes under the adjacent arm.

A total of 1016 patients were randomized between June 1997 and December 1999; 48% of patients had node-negative disease and 16% were age 65 years or older.

After surgery, patients were randomized to receive four cycles of either standard-dose of anthracycline doxorubicin 60 mg/m2 and cyclophosphamide 600/mg/m2 (n=510) or Taxotere 75 mg/m2 and cyclophosphamide 600mg/m2 (n=506), administered by intravenous infusion every three weeks. After chemotherapy was completed, patients were treated with radiation therapy if indicated. Patients with hormone receptor positive disease also received hormonal therapy (tamoxifen).

In the TC group, there were 88 DFS events (17%) and 58 deaths (12%). The AC group had 118 DFS events (23%) and 84 deaths (17%). Exploratory analyses showed benefit of TC irrespective of age, hormonal status or Her2 status.

Grade 3-4 neutropenia occurred in 60% of younger (<65 years) and 52% of older (≥65 years) women in the TC group, and in 54% and 59% of younger and older women, respectively, in the AC group.

Among younger patients, the frequencies of Grade 3-4 febrile neutropenia were 4.4% with TC and 2.3% with AC, while in older patients the frequencies were 7.7% and 3.7% for TC and AC, respectively. Grade 3-4 nausea was less common among women in both age groups treated with TC (<65: 2%, ≥65: 3%) than those given AC (<65: 7%, ≥65: 5%). In the TC group, additional Grade 3-4 adverse events reported among women <65 and ≥65 were fever in 4% and 6% and infection in 7% and 6%, respectively, while in the AC arm the rates of Grade 3-4 fever were 3% and 4 % and Grade 3-4 infections were 10% and 2 % for younger and older women, respectively.

Drug Combination Tested For B.C. Brain Metastases

A combination of a "targeted" therapy and chemotherapy shrank metastatic brain tumors by at least 50 percent in one-fifth of patients with aggressive HER2-positive breast cancer, according to data presented by Dana-Farber Cancer Institute investigators at the San Antonio Breast Cancer Symposium.

Lapatinib (Tykerb) and capecitabine (Xeloda) were paired in an extension of a phase II clinical trial in which lapatinib given alone shrank brain metastases significantly in six percent of 241 patients.

In the extension trial, capecitabine was added to lapatinib in 49 patients whose metastases had progressed while on treatment. With the combination therapy, brain metastases shrank by 20% or more in 18 patients (37%) and shrank by at least 50% in 10 patients (20%), said Nancy Lin, of Dana-Farber's Breast Oncology Center.

"Very few medications have shown activity in the treatment of brain metastases, particularly in HER-

2-positive metastatic breast cancer patients," said Lin, who led the study with Eric Winer, director of the Dana-Farber Breast Oncology Center. "Therefore, these data are quite encouraging, and further studies are warranted."

Lapatinib is an oral small-molecule drug from GlaxoSmithKline that is approved along with capecitabine for treating patients with advanced or metastatic breast cancer whose tumors are driven by the abnormal growth signal, HER-2, and who have already undergone therapy including trastuzumab (Herceptin), a taxane drug, and an anthracycline compound. Lapatinib, like trastuzumab, blocks the HER-2 signal.

Up to one-third of women with advanced, HER-2-positive breast cancer may develop metastases to the brain.

"Although radiation treatment is often effective, as women live longer with metastatic cancer, some develop worsening of brain metastases despite radiation," said Lin. "Because cancer in the brain can have a major impact on quality of life, it is important to have treatment options to address this problem."

The study was sponsored in part by GlaxoSmithKline.

Sunitinib May Be Associated With Cardiac Toxicity

Another FDA-approved targeted cancer drug, sunitinib (Sutent, Pfizer), may be associated with cardiac toxicity, report researchers at Children's Hospital Boston, Dana-Farber Cancer Institute, and Thomas Jefferson University.

The collaborative study, led by Ming Hui Chen, a cardiologist at Children's who specializes in the cardiac health of cancer patients, appeared in the Dec. 15 issue of The Lancet, accompanied by an editorial.

Sunitinib is one of several new "smart" cancer drugs called tyrosine kinase inhibitors that targets specific signaling molecules inside cancer cells that aid cancer spread. Another "targeted" cancer therapy, imatinib (Gleevec, Novartis Pharmaceuticals), was reported last year in Nature Medicine to be associated with heart failure in patients with chronic myelogenous leukemia

Sunitinib was originally thought to be relatively free of cardiac side effects. However, a new retrospective analysis, focused on cardiovascular events, revealed a risk for heart failure, myocardial infarction and hypertension in 75 adult patients with imatinib-resistant, gastrointestinal stromal tumor (GIST) receiving multiple cycles of sunitinib in a phase I/II trial at Dana-Farber.

Of the 75, six (8%) developed symptoms consistent with moderate-to-severe congestive heart failure, and two had heart attacks. In all, eight (11 percent) had some kind of cardiovascular event while receiving sunitinib at FDA-approved or lower doses. Patients with preexisting coronary artery disease were more likely to develop cardiac problems. Nineteen percent of the 36 patients receiving the FDA-approved dose had clinically significant decreases in left ventricular ejection fraction, a measure of the heart's pumping ability.

In addition, 47% (35 of 75) developed hypertension. "Hypertension is a common side effect with certain cancer drugs, but the degree of hypertension—both the percentage of affected patients and the magnitude of increase in systolic blood-pressure—was notable," said Chen, who is also affiliated with Brigham and Women's Hospital, Dana-Farber Cancer Institute and Harvard Medical School.

Two patient biopsies revealed abnormalities in the heart cells' mitochondria (the structures responsible for energy production). Further studies, led by Maria Rupnick, of the Children's Hospital Boston Vascular Biology Program, and Thomas Force, from the Center for Translational Medicine and Division of Cardiology at Jefferson, examined heart-muscle cells from mice who had received the equivalent of a human dosage of sunitinib alone, and found direct evidence of cardiotoxicity.

"Early identification of cardiac side effects is an important part of keeping patients on life-saving cancer therapy over the long-term," said Chen. "In this study, the cardiac dysfunction and hypertension were usually medically manageable. Most patients were able to resume sunitinib therapy following temporary withholding of drug, addition of cardiac medications and/or dose adjustment."

"This sunitinib study highlights potential concerns with agents that are 'multi-targeted,' meaning they inhibit multiple factors involved in cancer progression," said Force, who led the study of imatinib patients published in Nature Medicine last year. "Some of these factors may also play important roles in maintenance of proper heart function, and their inhibition by cancer drugs could have adverse effects on the heart."

"The most important element of this new work is the close, creative collaboration between our medical oncology and cardiology teams," said George Demetri, a co-author on the paper and director of the Ludwig Center at Dana-Farber Cancer Institute and Harvard Medical School. "As our molecular targeting involves more pathways, we can inform one another's fields and

identify side effects early by working together across traditional disciplinary boundaries."

BRCA Carriers Live Longer Than Those With Normal Gene

Israeli investigators have found that Ashkenazi Jewish women with ovarian cancer who have mutations in the BRCA1 or BRCA2 genes lived significantly longer than Ashkenazi Jewish ovarian cancer patients without these mutations. After up to nine years of follow-up, BRCA1/2 mutation carriers were 28 percent less likely to die from the disease, even though women with the BRCA mutations are significantly more likely to develop ovarian and breast cancers. The study is published Jan. 1 in the Journal of Clinical Oncology.

"These findings are encouraging news for BRCA mutation carriers," said Siegal Sadetzki, head of the Cancer & Radiation Epidemiology Unit at the Gertner Institute, Chaim Sheba Medical Center in Tel Hashomer, Israel, and the study's senior author. "It's possible that patients with these mutations respond better to chemotherapy. Hopefully, once we learn more about the mechanisms of this response, tailoring individual treatment will further improve survival."

Normal BRCA1/2 genes control cell growth. Mutations in these genes, which are more common among Ashkenazi Jewish women (Jewish women of Eastern European descent) than in the general population, increase the risk of breast and ovarian cancers.

In one of the largest studies of this topic to date, the researchers from the National Israeli Study of Ovarian Cancer compared five-year survival between 213 Ashkenazi ovarian cancer patients with BRCA1/2 mutations ("carriers") and 392 Ashkenazi ovarian cancer patients without the mutations ("non-carriers").

After five years, 46 percent of the carriers were still alive, compared with 34.4 percent of the non-carriers. Median survival was 53.7 months for carriers and 37.9 months for non-carriers. The differences in survival were most pronounced for women diagnosed with more advanced disease (stage III or IV), with five-year survival rates of 38.1 percent for carriers and 24.5 percent for non-carriers. These findings persisted after controlling for other factors that influence ovarian cancer survival, such as patient age and some biological features of the tumor.

The researchers also analyzed ovarian cancer survival according to whether women had a BRCA1 or a BRCA2 mutation. Women with BRCA1 mutations lived a median of 45.1 months, and women with BRCA2 mutations lived a median of 52.5 months.

Multiple Myeloma:

Rev/Vel/Dex Response Rate High In Phase I/II Study

A new combination of bortezomib (Velcade) and two other drugs is showing a very high response rate in patients newly diagnosed with multiple myeloma, a team headed by Dana-Farber Cancer Institute investigators reported at the annual meeting of the American Society of Hematology.

The three-pronged regimen of Velcade, lenalidomide (Revlimid) and dexamethasone—referred to as Rev/Vel/Dex—has achieved an overall response rate of 98 percent in 42 patients evaluated in a phase I/II trial, said Paul Richardson, of Dana-Farber and the study's principal investigator. He added that 52 percent of the patients had high quality responses (very good partial response or better), with 30 percent achieving complete response to date.

"These may be some of the best response rates we've seen to date with up-front therapies, and although these are preliminary results, they are extremely promising," Richardson said. The patients were previously untreated.

Velcade is a proteasome inhibitor that blocks the myeloma cells' waste disposal system, creating an accumulation of toxic compounds that poison the cell. Revlimid is a chemical relative of thalidomide that affects several pathways in cancer cells, including immune mechanisms and blood vessel growth to tumors. Dexamethasone is a steroid hormone that counters inflammation and is used to treat hematologic malignancies such as myeloma. Studies leading to the trial of the three drugs in combination were carried out at Dana-Farber.

While these are the first results from trials of Rev/Vel/Dex given as initial, first-line therapy, the combination has already been shown effective for multiple myeloma patients who relapsed following successful treatment or who had not responded to standard therapies.

Richardson also reported preliminary data from a multicenter phase II trial of the combination in relapsed or refractory myeloma. "These data confirm the favorable side effect profile," said Richardson, "and the response rate of 72 percent—including complete, partial, and minor responses—is very encouraging."

The responses appear to be holding up well, with a duration of more than one year for some patients to date. Both trials will continue to enroll patients, and final results are expected next year.

FDA Approves Genetic Test For Breast Cancer Patients

The U.S. Food and Drug Administration has approved a test that helps in assessing the risk of tumor recurrence and long-term survival for patients with relatively high-risk breast cancer. The TOP2A FISH pharmDx is the first approved device to test for the TOP2A (topoisomerase 2 alpha) gene in cancer patients.

The TOP2A gene plays a role in DNA replication. The TOP2A FISH pharmDx test uses fluorescently labeled DNA probes to detect or confirm gene or chromosome abnormalities, a technology known as fluorescent in situ hybridization (FISH).

The recurrence of cancer depends partly on certain genes whose activity may be altered by changes in the number of gene copies in the tumor. Changes in the TOP2A gene in breast cancer cells mean there is an increased likelihood that the tumor will recur or that long-term survival will be decreased.

"When used with other clinical information and laboratory tests, this test can provide health care professionals with additional insight on the likely clinical course for breast cancer patients," said Daniel Schultz, director of FDA's Center for Devices and Radiological Health. "It can also provide valuable information to assist health care providers and patients in better understanding the biology of breast cancer disease."

The test is suitable for breast cancer patients who are premenopausal or for whom tumor characteristics, such as tumor size or lymph node involvement, suggest a higher likelihood of tumor recurrence or decreased survival.

The FDA reviewed evidence that the test has been properly validated for its intended use.

The product was studied in Danish patients who were treated with chemotherapy after removal of a breast tumor. The test is conducted on a small piece of the removed tumor. The removed piece is stained with the FISH chemicals and studied under a microscope.

The company submitted data from a study using tumor samples and clinical data from 767 patients with high risk tumors at 21 centers in Denmark. These studies confirmed that the test was useful in estimating time to local or distant recurrence and overall survival in women who received certain chemotherapy regimens assisting in the treatment of the disease.

The product is manufactured by Dako Denmark A/S (Glostrup, Denmark).

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 II

Phase II Study of AZD6244 in Relapsed or Refractory AML. University of Chicago, protocol 7925, Odenike, Olatoyosi, phone 773-702-6783.

Phase II Study of Fluoroestradiol as a Marker of Hormone Sensitivity of Metastatic Breast Cancer. University of Washington, protocol 8052, Mankoff, David, phone 206-288-2173.

Multicenter Phase II Study of Belinostat (PXD101) in Previously Chemotherapy Treated Thymoma and Thymic Carcinoma. NCI, protocol 8174, Giaccone, Giuseppe, phone 301-402-3415.

Phase II Trial of Irinotecan and AZD2171 in Patients with Metastatic Colorectal Cancer After Progression on FOLFOX Plus Cetuximab or FOLFOX Plus Bevacizumab and Cetuximab. Cancer and Leukemia Group B, protocol CALGB-80502, O'Neil, Bert, phone 919-966-4431.

Phase II Trial of Image Guided Preoperative Radiotherapy for Primary Soft Tissue Sarcomas of the Extremity. Radiation Therapy Oncology Group, protocol RTOG-0630, Wang, Dian, phone 414-805-4496.

Phase III

Endocrine Therapy in Combination with Anti-VEGF Therapy: A Randomized Double-Blind, Placebo-Controlled Phase III Trial of Endocrine Therapy Alone or Endocrine Therapy Plus Bevacizumab for Women with Receptor-Positive Advanced Breast Cancer. Cancer and Leukemia Group B, protocol CALG-40503, Dickler, Maura, phone 646-888-4560.

Phase III Randomized Trial of Chemotherapy with or without Bevacizumab in Patients with Recurrent or Metastatic Head and Neck Cancer. Eastern Cooperative Oncology Group, protocol E1305, Argiris, Athanassio, phone 412-648-6575.

Intergroup Phase III Randomized Controlled Trial Comparing Melphalan, Prednisone and Thalidomide Versus Revlimid in Newly Diagnosed Multiple Myeloma Patients Who Are Not Candidates for High Dose Therapy. Eastern Cooperative Oncology Group, , protocol E1A06, Stewart, Alexander, phone 480-301-4411.