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THE
CLINICAL CANCER LETTER
Cancer research news for clinicians

ASCO Annual Meeting:

Two Studies Advance The Treatment Of Early-Stage And Later Breast Cancer

Two major studies that advance the treatment of both early and advanced breast cancer were presented at the American Society of Clinical Oncology annual meeting earlier this month.

A plenary study found that giving zoledronic acid (Zometa), a drug used to treat bone metastases and recently approved to treat osteoporosis, to premenopausal women undergoing ovarian suppression and hormone therapy significantly reduces the risk of recurrence in early-stage breast cancer.

A late-breaking study found that adding bevacizumab (Avastin) to docetaxel (Taxotere) slows disease progression for patients newly diagnosed

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Clinical Trials:

Phase III BETH Study Combining Avastin And Herceptin Open For Enrollment

A new international study for women with HER2-positive breast cancer is open for enrollment.

The pivotal BETH (BEvacizumab and Trastuzumab Adjuvant Therapy in HER2-positive Breast Cancer) study is a phase III clinical trial investigating the benefits of combining two monoclonal antibodies, the anti-angiogenic, bevacizumab (Avastin) and the targeted therapy trastuzumab (Herceptin), with chemotherapy for the treatment of patients with early stage HER2-positive breast cancer.

"Trastuzumab is already the standard of care across all stages of HER2-positive breast cancer and has a proven survival benefit. Bevacizumab has been shown to be of benefit when given in combination with chemotherapy for the treatment of metastatic breast cancer," said Dennis Slamon, director of clinical/translational research at the University of California, Los Angeles Jonsson Comprehensive Cancer Center and principal investigator, Cancer International Research Group. "The design of the BETH clinical trial is based on the preclinical and early clinical work from the Slamon/TRIO Laboratories at UCLA. We are looking forward to investigating the additional benefit to patients of combining these two treatments with chemotherapy in the treatment of early breast cancer."

"Despite treatment advances, over 400,000 women worldwide still die from breast cancer every year, so striving to improve treatment outcomes remains critical," said Norman Wolmark, chairman of the Department of

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Advances In Breast Cancer Treatment Presented At ASCO

(Continued from page 1)

with locally advanced or metastatic breast cancer. This study adds to previous findings on bevacizumab for treating breast cancer.

"We have a multitude of therapies for women with breast cancer, but continue to need new treatments that are more effective and have fewer side effects," said Eric Winer, professor of medicine at Harvard Medical School and director of the Breast Oncology Center at Dana-Farber Cancer Institute. "Our goal is to prevent recurrence and prolong survival for patients with early-stage breast cancer, and control disease and improve survival for patients with advanced disease."

Following are summaries of the research:

Zoledronic Acid Reduces Recurrence In Early Breast Cancer In Women Undergoing HT

Researchers report that zoledronic acid (Zometa), a drug used to treat bone metastases and recently approved to treat osteoporosis, also lowers the risk of breast cancer recurrence in premenopausal patients with early-stage disease who have undergone surgery and are receiving ovarian suppression and hormone therapy. All women in this multicenter phase III trial had cancer that was estrogen-receptor- or progesterone-receptor-positive.

Recent studies have shown that zoledronic acid, a bisphosphonate drug, can reduce bone loss caused by cancer treatments. Preclinical research suggested the drug might also have an anticancer effect.

"It's very exciting to find that in addition to preventing bone loss in women undergoing adjuvant endocrine therapy for breast cancer, zoledronic acid can also reduce the likelihood that breast cancer will return in some women," said Michael Gnant, a professor of surgery at the Medical University of Vienna, the president of the Austrian Breast and Colorectal Cancer study group, and the study's lead author. "Future research will focus on optimizing the administration schedule and the dose, and determining which patients will benefit the most from treatment with zoledronic acid."

The study enrolled 1,803 patients who were undergoing drug-induced ovarian suppression (using goserelin), who previously had surgery to remove the primary tumor and whose cancer had spread to ten or fewer lymph nodes. The study had four arms: treatment with the hormone therapies tamoxifen or anastrozole, with or without zoledronic acid. Tamoxifen is given as a standard adjuvant treatment after surgery in both pre- and post-menopausal women who have hormone-responsive tumors. Anastrozole also is approved for hormone-responsive tumors, but only in post-menopausal women, a condition that ovarian suppression with goserelin simulates.

The study's primary endpoint was disease-free survival — the length of time after treatment in which no disease is found. After a median follow-up of 60 months, the researchers found that hormone therapy plus zoledronic acid reduced the risk of relapse by 35 percent compared with hormone therapy alone. They did not find a significant difference between the two hormone therapies. The treatment was well tolerated in all four groups and there were no unexpected side effects.

Bevacizumab Slows Advanced Breast Cancer

A large, international trial has shown that adding the targeted therapy bevacizumab (Avastin) to the chemotherapy drug docetaxel (Taxotere) slows disease progression in patients without prior chemotherapy for locally advanced or metastatic breast cancer. Bevacizumab targets the blood vessels that feed tumors and is known as an antiangiogenic drug.

Previous studies have shown that adding bevacizumab to paclitaxel (Taxol, a taxane chemotherapy agent similar to docetaxel) for patients with metastatic breast cancer doubles progression-free survival. This is the first phase III trial to evaluate bevacizumab in combination with docetaxel, a drug that is used much more commonly in Europe, Asia, and Australia, while paclitaxel is used more often in the United States.

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In February, the U.S. Food and Drug Administration approved bevacizumab in combination with paclitaxel for the treatment of newly diagnosed metastatic breast cancer; the drug was previously approved to treat colorectal cancer.

"This study shows the antiangiogenic approach to treating breast cancer is effective, regardless of which taxane drug it is combined with," said David Miles, a professor and medical oncologist at the Mount Vernon Cancer Centre and the study's lead author. "We found it does not add a great deal to the toxicity of chemotherapy, which should be reassuring to physicians recommending this course of treatment."

In the current study, the AVADO trial, 736 patients were randomized among three arms: placebo plus docetaxel, a higher dose of bevacizumab (15 mg/kg) plus docetaxel, and a lower dose of bevacizumab

(7.5 mg/kg) plus docetaxel. The higher dose was the standard that was established in earlier breast cancer studies; the lower dose was the standard used to treat colorectal cancer.

After a median follow-up of 11 months, investigators found that patients in the low-dose group were 21 percent less likely to have their disease progress, compared with those who received docetaxel alone. Patients in the high-dose group were 28 percent less likely to have their disease progress compared with those who received docetaxel only. The percentage of patients who had their tumors shrink was 44.4 percent in the placebo plus docetaxel group, 55.2 percent in the low-dose bevacizumab group, and 63.1 percent in the high-dose group. Because of the number of patients in the trial, it was not possible to statistically compare the two doses with each other.

Patients in the two bevacizumab groups had a slightly higher rate of severe side effects: 74.8 percent in the low-dose group and 74.1 percent in the high-dose group, compared with 67.0 percent in the docetaxel-alone group. The most common side effect attributed to bevacizumab was high blood pressure, which was treatable with medication. Severe bowel perforation, a toxicity seen in some other bevacizumab trials, occurred in few patients: two patients in the placebo arm, and one patient in each of the experimental arms.

Highlight of other breast cancer studies from ASCO follow.

Phase II Study of Iressa

Gefitinib, the once-promising drug formerly approved as a second line treatment for lung cancer, also known as Iressa, enhanced the effectiveness of hormonal therapy for the treatment of specific types of metastatic breast cancer, according to a phase II clinical trial led by researchers at M. D. Anderson Cancer Center.

These findings are surprising and represent the first positive study for Iressa in breast cancer, as well as for the entire class of drugs known as epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors, said Massimo Cristofanilli, the study's principal investigator.

"We initiated this study in 2003 with hopes of reducing the resistance to hormonal therapy," said Cristofanilli. "There was a lot of preclinical work indicating that, in fact, resistance to hormonal therapy is strongly associated with an activated EGFR pathway. Also, EGFR over-expression has been associated with endocrine resistance. If there's a double blockage of the EGFR and the estrogen receptor, you may achieve better control of the disease."

The study enrolled 93 women from 30 centers in the U.S. and Latin America, with M. D. Anderson enrolling 20 patients. All of the women were newly diagnosed with metastatic breast cancer and were hormone receptor positive and estrogen receptor HER-2 negative. Patients were randomized to receive the aromatase inhibitor Arimidex (1 milligram) and Iressa (250 milligram) daily or Arimidex and placebo. The primary endpoint was progression-free survival.

When the study was unblinded, the researchers were surprised by the distinct findings: in the women who received Arimidex and Iressa, progression-free survival was 14.5 months, compared to 8.2 months in the women who did not receive Iressa, representing a 45 percent reduction in risk.

Also, of the women taking the combination, 47 percent had stable disease for more than 24 weeks and 49 percent had a clinical benefit. In contrast, 22 percent of the women had taking Arimidex alone had stable disease for more than 24 weeks and 34 percent had a clinical benefit.

Patients in the combination arm did have a higher rate of adverse events, but Cristofanilli notes that overall Iressa was very well tolerated.

"To see such a difference in such a small subset of patients was tremendously surprising," said Cristofanilli. "These findings show the possibility of adding a targeted therapy such as Iressa or others in the EGFR drug class to improve the benefit for hormonal therapy, giving another option for women who are hormone receptor positive, Her-2 negative with metastatic disease."

About 60 percent of women with breast cancer are hormone receptor positive and Her-2 negative, said

Cristofanilli.

Iressa, a once-daily, oral tablet, was the first in a new class of anti-cancer drugs known as epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors, to become commercially available. Iressa received FDA approval in 2003 as a single agent treatment for patients whose advanced lung cancer has continued to progress despite treatment with platinum-based and docetaxel chemotherapy.

However, in 2005, after a large international study resulted in negative findings and reported numerous negative side effects, the drug's labeling was altered by the FDA. Only cancer patients who had already taken the medicine and whose physician believed it was helping them were allowed to receive the drug. No new lung cancer patients were given the drug after this time.

During this period, Iressa was being tested in clinical trials in a number of cancer types, including breast cancer. Other breast cancer trials studying Iressa, either as a single agent or when combined with chemotherapy, were mostly negative.

These negative findings impacted the accrual of the Arimidex-Iressa breast cancer study, said Cristofanilli. The study fell well short of its accrual goal of 174 women.

"Still, there's significant clinical relevance to our findings. Of course, I would advise that physicians not rush to put metastatic breast cancer patients who are hormone receptor positive and estrogen receptor negative on other drugs in this class that are readily available," said Cristofanilli. "Rather, this study should serve as a proof-of-concept. With our results, there should be a renewed interest in this class of drugs and hopefully follow-up studies in the adjuvant setting will be conducted."

Bone Density And Metastasis

Maintaining bone density could be a key to decreasing the spread of cancer in women with locally advanced breast cancer, according to research at Washington University School of Medicine in St. Louis.

Bones are common sites for the metastasis of breast cancer. Scientists found that women treated for stage II/III breast cancer who also received a bone strengthening drug were less likely to have breast tumor cells growing in their bones after three months. The bone-strengthening drug used was zoledronic acid, a drug that decreases bone turnover and reduces bone fractures in patients with osteoporosis.

"Tumor cells are continually being released from the primary tumor," says lead author Rebecca Aft, associate professor of surgery, faculty member of the Siteman Cancer Center and a Washington University breast surgeon at Barnes Jewish Hospital. "It is thought that the bone marrow harbors these cells and that these cells are likely to evolve into metastatic disease. We think that zoledronic acid changes the bone marrow so that cancer cells are unable to lodge there."

The researchers randomly assigned 120 women being treated for clinical stage II/III breast cancer to receive 4 milligrams of zoledronic acid intravenously every three weeks for one year, starting with their first cycle of chemotherapy, or to receive no zoledronic acid. Stage II/III cancer means the primary tumor has spread into lymph nodes or other areas near the breast.

At the time of diagnosis, none of the patients had evidence of metastatic disease on CT or PET scans. Bone marrow samples showed that about 40 percent of the patients had detectable breast tumor cells in the bone marrow.

Prior research has shown that women with even minuscule clusters of breast tumor cells, called micrometastases, in their bone marrow at the time of their diagnosis have an increased risk of developing large metastatic tumors later.

The researchers took bone marrow samples again three months and one year after treatment began. Only 23 percent of women who got zoledronic acid had tumor cells after three months compared to 36 percent of those who didn't get the drug. This result did not reach statistical significance.

Of women who started with no tumor cells in their bone marrow, 88 percent remained free of tumor cells in their bone marrow if they got zoledronic acid, compared to 70 percent of those who did not receive the drug. This result approached statistical significance. The one-year results are not yet available.

Women who receive chemotherapy for breast cancer have increased rates of bone turnover, which can release growth factors and produce a favorable environment for cancer cells, Aft said. The suppression of bone turnover by zoledronic acid or other bisphosphonate drugs could make bones less friendly surroundings for cancer.

"We found that patients who are negative for tumor cells in bone marrow have a very good chance of staying negative if they take zoledronic acid," Aft said. "If longer follow up shows that women without tumor cells in their bones do not go on to develop metastatic disease, then it would be reasonable to say that bisphosphonates will likely benefit women with locally advanced breast cancer."

Metformin Increases Pathologic CR In Breast Cancer Patients With Diabetes

Metformin, the common first-line drug for type 2 diabetes, may be effective in increasing pathologic complete response rates in diabetic women with early stage breast cancer who took the drug during chemotherapy prior to having surgery, paving the way for further research of the drug as a potential cancer therapy, according to researchers at M. D. Anderson Cancer Center.

The retrospective study is the first clinical research observation of the diabetes drug as a potential anti-tumor agent. The findings were presented by Sao Jirlerspong, a fellow, and Ana Gonzalez-Angulo, assistant professor, both in M. D. Anderson's Department of Breast Medical Oncology.

Metformin, an oral medication, is the most common drug prescribed for type 2 diabetes. It's most often given to diabetic patients who are obese or have insulin resistance.

The authors decided to conduct the research after a large, intriguing epidemiologic study published last year showed that patients with diabetes who took metformin had lower incidences of cancer as well as better outcomes.

"Metformin has a novel mechanism of action. There have been a number of papers published recently that describe its action through activation of the AMP kinase pathway, which is a cellular energy sensor of the cells and potentially important pathway for the development of cancer," said Jiralerspong.

"The other interesting aspect is that Metformin works by decreasing the amount of insulin- resistance in diabetics and insulin seems to be a growth factor for cancer," said Gonzalez-Angulo.

Using the M. D. Anderson Breast Medical Oncology database, Gonzalez-Angulo, Jiralerspong and their team identified 2,529 women with early-stage breast cancer who received chemotherapy in the neoadjuvant setting, before surgery. Of the patients, 2,374 were non-diabetic, 68 were diabetic but not taking metaformin and 87 were diabetic and taking the drug. The study's endpoint was pathologic complete response, or the absence of cancer at the time of surgery.

The researchers found that the pathologic complete response rates in the diabetic breast cancer patients taking Metformin was 24 percent, three times higher than the rates in diabetic patients not taking the drug, 8 percent. In the non-diabetic women, the pathologic complete response rate was 16 percent. After adjusting for other factors, the researchers found that metformin was an independent predictor of pathologic complete response in diabetic patients.

M. D. Anderson plans to open a clinical trial with metformin in combination with hormonal therapy for metastatic breast cancer patients who are obese. The study will be led by Francisco Esteva, associate professor in the Department of Breast Medical Oncology.

Oral Drug Doesn't Benefit Older Women With Early-Stage Breast Cancer

A study led by Hyman Muss, of the University of Vermont College of Medicine, found that the oral chemotherapy drug capecitabine was inferior to standard chemotherapy as adjuvant therapy in older women with early-stage breast cancer.

Capecitabine is approved for treatment of metastatic breast cancer or breast cancer that has recurred after other treatments, in combination with other chemotherapy agents. It was thought that capecitabine might be an equally effective but gentler drug for older patients, who are more likely to have other health problems that could make cancer treatment more difficult to tolerate. Capecitabine is also being evaluated in trials as an adjuvant treatment for early-stage breast cancer, either alone or in combination with other agents.

This randomized trial included 633 women with early-stage breast cancer who were 65 or older and had already had surgery to remove their tumors. The investigators randomized patients into two treatment arms—326 patients received standard chemotherapy and 307 received capecitabine. After a median follow-up of 2.4 years, the investigators found that patients in the capecitabine arm were 2.4 times more likely to suffer a relapse and 2.1 times more likely to die than those receiving standard treatment.

Clinical Trials:

Phase III Study Of Avastin And Herceptin Enrolls Patients

(Continued from page 1)

Human Oncology at the Allegheny General Hospital, and principal investigator, NSABP Foundation Inc.

In BETH, patients will be randomized to a regimen of chemotherapy (either 6 cycles of docetaxel/carboplatin or 3 cycles of docetaxel, followed by 3 cycles of FEC) plus trastuzumab with or without bevacizumab.

BETH was developed through the collaborative efforts of the National Surgical Adjuvant Breast and Bowel Project and the Cancer International Research

Group. The study will be led by the two groups and will recruit approximately 3,500 patients. The primary outcome measure of BETH will be invasive disease-free survival. Secondary endpoints for the study include disease-free survival, overall survival, safety, and tolerability.

Bevacizumab and trastuzumab are used in the treatment of women with breast cancer; bevacizumab for metastatic breast cancer and trastuzumab for both early and late HER2-positive breast cancer. This is the first phase III trial to evaluate combining the two therapies in treating early stage breast cancer.

CIRG is a not-for-profit research organization with offices based in Paris, France, and Alberta, Canada. Recently, CIRG has partnered with the UCLA-based investigator network of Translational Oncology Research International, to form TRIO (Translational Research in Oncology), which includes the Slamon/TRIO Laboratories at UCLA. Slamon and fellow scientists have developed and adapted preclinical models which allow for the validation of molecular markers, the preclinical assessment of new biologic agents and the characterization of an agent's mechanisms of action. This preclinical work, in turn, generates the clinical hypotheses for the group's future cancer trials in patients.

NSABP is an NCI-supported clinical trials cooperative group based in Pittsburgh.

Brachytherapy Prevents Endometrial Cancer Return

The first phase III study of its kind has found that vaginal brachytherapy, in which a radioactive cylinder is inserted into the vagina, is as effective at preventing the recurrence of higher-risk endometrial cancer as external beam radiation therapy, has fewer side effects and results in a better quality of life for patients.

"Based on this study, we expect that vaginal brachytherapy will be adopted as the new standard of care for patients with this type of endometrial cancer," said Remi Nout, a resident in radiation oncology in the department of clinical oncology at Leiden University Medical Center and the study's lead author. "This treatment is simpler and just as effective as external beam radiation, and it allows patients to have a better quality of life both during and after treatment. This new strategy will make treatment and recovery for many patients much more manageable moving forward."

For high-intermediate risk disease—which is determined by the tumor's grade and stage and the patient's age—the standard treatment has been surgery followed by external beam radiation therapy. Brachytherapy is currently used in combination with external beam radiation for more advanced disease. Patients with low-risk disease are treated with surgery alone.

This multicenter Dutch study randomized 427 patients with high-intermediate risk endometrial cancer into two arms: 214 patients received external beam pelvic radiotherapy and 213 received vaginal brachytherapy. All patients had previously undergone surgery to remove their uteruses and ovaries. At three years of follow-up, rates of vaginal, pelvic, and distant relapse were 0 percent, 1.3 percent, and 6.4 percent in the brachytherapy group and 1.6 percent, 0.7 percent, and 6.0 percent in the external beam radiotherapy group. There were no significant differences in overall survival (90.4 percent vs. 90.8 percent) or progression-free survival (89.5 percent vs. 89.1 percent).

Patients who received brachytherapy, however, reported a lower level of side effects than patients who received external beam radiotherapy. The most common side effect was diarrhea. After completion of radiotherapy, 22 percent of external beam radiotherapy patients reported moderate to severe diarrhea, compared to 6 percent in the vaginal brachytherapy group. As a result, 13 percent of external beam radiotherapy patients reported moderate to severe limitation in their daily activities due to bowel problems, compared to 5 percent in the vaginal brachytherapy group. Although these side effects gradually decreased over time, two years after treatment 6 percent of external beam radiotherapy patients still reported moderate to severe diarrhea, compared to 1 percent in the vaginal brachytherapy group, which resulted in 5 percent and 2 percent moderate to severe limitation in daily activities due to bowel problems, respectively.

Physicians reported significantly higher rates of gastrointestinal toxicity during external beam radiotherapy: 35 percent had mild diarrhea or cramping and 19 percent had moderate diarrhea greater than five times a day during external beam radiation therapy, compared to 12 percent and 1 percent for brachytherapy.

Following are highlights of other studies presented at the ASCO meeting that pointed to improvements in quality of life:

Gemcitabine Improves Overall Survival In Early-Stage Pancreatic Cancer

A large, multicenter study has shown that the

chemotherapy drug gemcitabine (Gemzar) more than doubles overall survival in patients who have undergone surgery for pancreatic cancer. The CONKO-001 trial is the first large-scaled phase III study to show a benefit for any chemotherapy agent given to early-stage pancreatic cancer patients after surgery to remove their tumors.

Gemcitabine is the standard treatment for pancreatic cancer that is too advanced for surgery. The CONKO-001 study examined whether it is beneficial earlier in the course of the disease. Previous results from this study, presented at the ASCO annual meeting in 2005, showed that adjuvant gemcitabine improves disease-free survival (the length of time that no disease is found after treatment); investigators continued to follow these patients in order to determine whether the drug also improves overall survival.

"The ultimate goal of adjuvant therapy is improving the cure rate, and we have shown that this treatment more than doubles the overall survival five years after treatment," said Hanno Riess, a professor at Charité University Medical School in Berlin and the leader of the CONKO study group. "Based on the earlier results of this study, this regimen is already more widely used in both Europe and the United States. These findings can reassure physicians that the drug is also extending lives."

The trial randomized 368 patients to receive post-operative gemcitabine or undergo observation, which included no specific anticancer treatment. All patients first had complete surgical removal of their tumor, with no detectable macroscopic disease remaining. Because pancreatic cancer is usually diagnosed at a late stage, only about 15 to 20 percent of patients are diagnosed at an earlier stage and are eligible for surgery.

Estimated disease-free survival at three and five years, respectively, was 23.5 percent and 16.5 percent for the gemcitabine group versus 7.5 percent and 5.5 percent for the observation group. Overall survival at three and five years was 36.5 percent and 21.0 percent for the gemcitabine group, versus 19.5 percent and

9.0 percent for the observation group. Gemcitabine was well-tolerated among patients and there were no differences in toxicity between the groups, except for white blood cell and platelet counts, which were lower in the gemcitabine group.

Additional studies are already underway comparing treatment with gemcitabine alone to treatment with gemcitabine plus the targeted therapies erlotinib (Tarceva) or sorafenib (Nexavar) in patients who have undergone successful surgical resection of their cancer.

Everolimus Improves Progression-Free Survival In Advanced Kidney Cancer

A multicenter study has found that the experimental targeted therapy everolimus (Cetican, RAD001) delays cancer progression in patients with metastatic kidney cancer that has progressed despite treatment with other targeted therapies.

Everolimus is administered orally and targets the mTOR protein, which regulates cell division and blood vessel growth in cancer cells. It is being evaluated for the treatment of several other cancers and is currently approved as an immunosuppressant to prevent the rejection of organs after transplant.

"This study has given us a new and clearly useful tool for treating renal cell tumors. It's an important step forward for patients living with this disease," said Robert Motzer, an attending physician at Memorial Sloan-Kettering Cancer Center and the study's lead author. "In the future, kidney cancer is likely to be managed as a chronic disease with treatments including this one."

All patients in this study had the most common type of kidney cancer, renal cell carcinoma with a clear cell component. They also had been previously treated with sunitinib and/or sorafenib, which target a different receptor commonly found in kidney tumors (vascular endothelial growth factor, or VEGF), but had stopped responding.

Patients were randomized to receive everolimus (272 patients) or placebo (138 patients), plus best supportive care (which can include measures such as palliative radiation therapy). After six months, 26 percent of patients in the everolimus group had not progressed, versus only 2 percent in the placebo group. The difference in median progression-free survival (the average time it took for the cancer to get worse) was 4 months for everolimus, versus 1.9 months for placebo.

The most common side effects for patients receiving everolimus were mouth ulcers (36 percent, vs. 7 percent in the placebo group), anemia (28 percent vs. 15 percent) and weakness (28 percent vs. 20 percent). The instances of severe (grade 3 or 4) toxicity were 5 percent or lower for each side effect.

Clinical Trials: Best Kept Secret?

Patients Report Clinical Trials Not Offered By Physician

Why do so few cancer patients take advantage of clinical trials? One reason is they are not hearing that such trials are a treatment option for them, according

to a study by researchers at the Paul P. Carbone Comprehensive Cancer Center of the University of Wisconsin School of Medicine and Public Health.

Lead investigator Timothy Wassenaar presented the findings at the annual meeting of the American Society of Clinical Oncology in Chicago earlier this month.

About 60 percent of newly diagnosed cancer patients say they were never told that such clinical trials were a treatment option for them, he said.

"It could be that newly diagnosed patients don't hear anything else from the physician after they're told they have cancer. It doesn't necessarily mean that physicians aren't giving patients the information," Wassenaar noted as one possible explanation for the findings.

Earlier studies found that only 2 to 4 percent of new adult cancer patients participate in clinical trials. The Carbone Cancer Center, Wisconsin's only comprehensive cancer center, offers 250 clinical trials a year. Seven hundred patients participated in clinical trials at the cancer center last year.

"The take-home message is that participating in clinical trials not only helps researchers and physicians learn about better ways to treat cancer. But all patients who participate in such trials get state-of-the-art cancer care," said Patrick Remington, associate director of UWCCC and co-investigator on the study.

Wassenaar and his team studied nearly 1,900 Wisconsin cancer patients. The patients had been diagnosed with one of four cancers including breast, colorectal, lung and prostate.

According to the study, 9.8 percent of breast cancer patients and 11 percent of both lung and colorectal cancer patients sign up for clinical trials. In contrast, only 2.5 percent of prostate cancer patients are likely to enroll.

Patients who have to travel distances for care, live in a rural setting, or are involved in cancer-specific support groups are more likely to participate in clinical trials. Patients who are not satisfied with their care are less likely to try clinical trials.

Wassenaar said more research is needed on exactly why many cancer patients don't participate in clinical trials and what methods might be more effective in communicating that clinical trials are a treatment option.

"One of the major barriers to participation in clinical trials was eliminated in Wisconsin last year with passage of a law that mandates insurance companies to cover costs of patients in clinical trials," said Remington. A total of 23 states have similar laws, according to the Council for Affordable Health Insurance.

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

Inhibition of DNA Methylation by 1-Hr Infusion of 5-aza-2'-Deoxycitidine (Decitabine) x 10 Days (M-F) with Escalating Doses of Sub-Q Pegylated Interferon-alpha 2B (PEG-Intron): A Phase I Study with Molecular Correlates. Nevada Cancer Institute, protocol 8224, Samlowski, Wolfram, phone 702-822-5215.

Phase I/II

Phase I/II Trial of IMC-A12 in Combination with Temsirolimus in Patients with Metastatic Breast Cancer. Mayo Clinic Rochester, protocol 8129, Ma, Cynthia, phone 314-362-9383.

Phase I and a Randomized Phase II Study of Maximal Angiogenic Blockade in Advanced Renal Carcinoma: Bevacizumab with or without MEDI-522. Southwest Oncology Group, protocol S0717, Ryan, Christopher, phone 503-494-8487.

Phase II

Phase II Randomized Study of Patients with Rising PSA at High-Risk of Progression after Primary Therapy to Assess the Clinical and Molecular Efficacy of the Enzastaurin - Bicalutamide Combination to Suppress the Adrogen Receptor Without Testosterone Ablation. Eastern Cooperative Oncology Group, protocol E1807, Ferrari, Anna, phone 212-731-5389.

Phase II Study of Oxaliplatin Capecitabine, Cetuximab and Radiation in PreOperative Therapy of Rectal Cancer. Southwest Oncology Group, protocol S0713, Leichman, Cynthia, phone 760-416-4860.

Other

Low Intensity Allogeneic Hematopoietic Stem Cell Transplantation Therapy of Metastatic Renal Cell Carcinoma Using Early and Multiple Donor Lymphocyte Infusions Consisting of Írolimus-Generated Donor Th2 Cells. NCI, Experimental Transplantation and Immunology Branch, protocol 8242, Fowler, Daniel, phone 301-435-8641.