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# ASCO Updates

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The annual meeting of the American Society of Clinical Oncology was held in Orlando from May 29 to June 2. The gathering attracted 30,000 cancer researchers, physicians, and representatives from pharmaceutical and biotechnology industries to learn the latest in cancer care, treatment, and prevention. Details can be found at [www.asco.org](http://www.asco.org) or ASCO's patient website, [www.cancer.net](http://www.cancer.net)

### PARP Inhibitors Successful Against Hard-to-Treat Breast Cancers

A new class of drugs called PARP inhibitors is getting some serious attention after a study in metastatic triple-negative breast cancer patients found that the agent BSI-201 significantly improved survival.

A phase II study randomly assigned 116 patients to receive chemotherapy (Gemzar [gemcitabine] and carboplatin) with or without intravenous BSI-201. For patients receiving the experimental agent, progression-free survival (the time before the tumor progressed) reached 6.9 months, compared with 3.3 months for the chemotherapy-alone group. Overall survival hit 9.2 months for the BSI-201 arm versus 5.7 months for patients not receiving the drug. Side effects were similar between the two groups, the most common of which were low blood counts.

A separate phase II study tested a different PARP inhibitor called olaparib as a single agent in patients with advanced breast cancer who have BRCA1 or BRCA2 mutations, a genetic alteration that predisposes a carrier to breast and ovarian cancers. In this single-arm trial, 11 of the 27 patients receiving the higher of the two doses used in the study had their tumors shrink by at least half. Side effects of the oral agent included mild nausea and fatigue.

PARP is an enzyme used by cancer cells to repair DNA damage—specifically the damage caused by chemotherapy. By inhibiting PARP, the cancer cells are more susceptible to the effects of treatment. PARP inhibitors are especially beneficial in patients who have deficient DNA repair systems, as is the case for those with mutations in BRCA1 or BRCA2.

A phase III study of BSI-201 in metastatic triple-negative breast cancer will launch at the end of June, said researchers.

### Zactima Delays Advanced Lung Cancer Growth

An international phase III trial found the investigational lung cancer drug, Zactima (vandetanib), significantly slowed the time a patient's advanced lung cancer progressed. The trial, which included nearly 1,400 patients who progressed on prior therapy, compared Taxotere (docetaxel) in combination with either placebo or Zactima.

While the data do not show an overall survival advantage, patients on the Zactima arm had a median progression-free survival of 17.3 weeks compared with 14 weeks with Taxotere alone. Zactima works by blocking both vascular endothelial growth factor, which is instrumental in blood vessel growth to the tumor, and the epidermal growth factor receptor, a protein that spurs malignant cell growth.

Common side effects with Zactima are diarrhea, rash, and neutropenia, which can increase the risk of infection. With the progression-free survival benefit demonstrated, AstraZeneca, the drug's manufacturer, is planning to submit the drug for Food and Drug Administration approval in the coming months. The drug is also being tested in thyroid cancer.

### Antidepressants Reduce the Effectiveness of Tamoxifen

Taking tamoxifen at the same time as certain drugs that treat depression and hot flashes may reduce the cancer drug's ability to prevent breast cancer recurrence. The offenders in the study—Paxil (paroxetine), Prozac (fluoxetine), and Zoloft (sertraline)—are part of a class of drugs that inhibit CYP2D6, an enzyme that converts tamoxifen to its active form.

A U.S. study found that after two years, 7.5 percent of women who took only tamoxifen had a recurrence, compared with 16 percent who took Paxil, Prozac, or Zoloft—drugs considered to be the most potent CYP2D6 inhibitors. That difference translates to a 120 percent increase in the risk of breast cancer recurrence. Patients taking the so-called weaker antidepressants, Celexa (citalopram), Lexapro (escitalopram), and Luvox (fluvoxamine), did not have an increased risk of recurrence.

However, a Dutch study presented at the meeting did not find that simultaneous use was unsafe, most likely because of the small number of patients in the study who took both drugs, said Julie Gralow, MD, of the Seattle Cancer Care Alliance, at a press briefing. (Gralow was not involved in either study.) The Dutch trial included less than half the number of patients in the U.S. study who took the drugs concurrently—150 versus 353 women. Other drugs to treat depression and hot flashes that do not inhibit CYP2D6 should be considered for tamoxifen patients, said Gralow.

### Herceptin Improves Survival in Gastric Cancer

The breast cancer drug Herceptin (trastuzumab) extends survival in certain gastric cancer patients by almost three months, according to a phase III international study.

Because research has shown that about 20 percent of gastric tumors overexpress HER2, investigators randomly assigned 594 patients with locally advanced, recurrent, or metastatic HER2-positive gastric cancer to receive chemotherapy (5-FU or Xeloda [capecitabine] and cisplatin) with or without Herceptin. Patients receiving Herceptin had a median overall survival of 13.8 months compared with 11.1 months in the chemotherapy-alone arm. For patients with the highest levels of HER2, median survival reached 16 months. Side effects were similar between the two arms, with no increased risk for heart damage, an effect sometimes seen with Herceptin.

“Based on these data, we should offer patients the option of [HER2] testing, and if they are HER2-positive ... we should then offer these patients Herceptin,” said lead researcher Eric Van Cutsem, MD, PhD, of the University Hospital Gasthuisberg in Belgium, at a press briefing.

The Food and Drug Administration approved Herceptin more than a decade ago for HER2-positive breast cancer. Roche, which markets Herceptin internationally, said in a statement that it plans to file the drug for approval in advanced HER2-positive gastric cancer.

### Therapeutic Vaccine Delays Lymphoma Recurrence

While follicular lymphoma frequently responds to chemotherapy and can have a long course, the disease is considered incurable because it almost always recurs. Researchers of a lymphoma trial hope that BiovaxID, a personalized vaccine, could help delay those recurrences.

The study included 117 patients who experienced at least a six-month remission after chemotherapy, and retained that remission until receiving either BiovaxID or a control vaccine. Each patient randomized to the BiovaxID arm was given a series of injections of a vaccine developed from their own cancer cells, making it a specialized targeted drug against the individual’s malignant B cells. After a median of nearly five years follow-up, BiovaxID improved cancer-free survival by 47 percent, delaying recurrence for more than a year, from 30.6 months to 44.2 months, when compared with the control vaccine. No major differences in side effects occurred between the two arms.

Researchers stressed the need for future studies, including combining the vaccine with targeted drugs such as Rituxan (rituximab), an agent that is now a standard of care for lymphoma.

### CA-125 Monitoring Not Helpful for Ovarian Cancer Survivors

Results from an international study challenge current practice of screening for ovarian cancer relapse. Currently, survivors undergo quarterly monitoring of CA-125, a protein that is predictive of ovarian cancer relapse. With early detection of recurrence, patients often begin treatment before symptoms manifest. However, a study showing that early treatment does not improve overall survival may change that tradition.

☒ For the first time, women can be offered informed choices after first-line chemotherapy. ☒

—Gordon Rustin, MD

The study looked at 529 ovarian cancer survivors who were in remission but whose CA-125 levels began to rise. Researchers found that the group who received treatment at the time their levels increased did not live longer than the group who received treatment after the onset of symptoms (these patients did not have their levels made available to the physician or patient). Patients with early treatment received therapy about four to five months sooner than the delayed treatment group, but this did not result in improved survival. In addition, the quality of life was lower in the group who received quarterly CA-125 testing, presumably because of anxiety about the results and because this group was exposed to more types of chemotherapy and longer treatment.

“For the first time, women can be offered informed choices after first-line chemotherapy,” said presenter Gordon Rustin, MD, of Mount Vernon Cancer Centre, during the presentation. Because early treatment does not result in a survival advantage or a longer remission, Rustin told doctors there is no benefit from early recurrence detection with routine CA-125 testing.

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