Targeted therapy extends progression-free survival of patients with advanced ovarian cancer

December 28 2011

Targeted drugs, which block or disrupt particular molecules involved in the growth of tumors, have been shown to be effective treatments against many types of cancer. A new phase 3 clinical trial conducted by the Gynecologic Oncology Group (GOG) showed that a targeted therapy called bevacizumab (Avastin) effectively delayed the progression of advanced ovarian cancer. Patients with newly diagnosed advanced ovarian cancer now typically undergo surgery and chemotherapy, but the new research suggests an additional avenue of treatment. The results of the trial appear in the December 29 issue of the *New England Journal of Medicine*.

"This approach can be looked upon as a third major component of treatment for ovarian cancer and related malignancies," says Robert A. Burger, MD, lead investigator on the GOG study and director of the Women's Cancer Center at Fox Chase Cancer Center. "We've had the combination of surgical management and cytotoxic chemotherapy for many years, but we haven't really seen anything else in terms of a fundamental class of treatment. This represents a new way for us to control the disease."

The placebo-controlled study, which was sponsored by the National Cancer Institute, enrolled 1,873 patients with previously untreated advanced disease from 336 sites, primarily in the United States, but also in Canada, South Korea, and Japan. The patients either had stage III

ovarian cancer that could not be entirely removed with surgery, or stage IV disease, and were randomly assigned to one of three groups. For patients who received bevacizumab with chemotherapy followed by bevacizumab for up to an additional 10 months, the median time until their cancer progressed was 14.1 months, compared to 10.3 months for patients in the control group, who received chemotherapy with a placebo and then continued with a placebo. The net effect was a 28% reduction in the risk of disease of ovarian cancer progression over time. Patients who received bevacizumab only with chemotherapy, but not afterward, had a median progression-free survival of 11.2 months.

The National Cancer Institute estimates that nearly 22,000 women were diagnosed with ovarian cancer in 2011, and more than 15,000 died of the disease. For patients diagnosed before the cancer has spread, the five-year relative survival rate is about 93 percent (relative survival measures survival of cancer only, independent of other causes of death). But ovarian cancer is insidious—early symptoms, like bloating, abdominal pain, and trouble eating, are typical of many illnesses and easily dismissed as non-threatening. Women often do not learn they have the disease until it's already spread. In 62 percent of new cases, the patient's cancer has metastasized to distant sites, and the five-year survival rate is just under 27 percent.

Bevacizumab is already FDA-approved for use against some types of colon, lung, kidney and brain cancers; its accelerated approval for metastatic breast cancer was recently revoked by the FDA. The drug acts by binding with vascular endothelial growth factor (VEGF), a protein produced by certain cancers that helps initiate the growth of new blood vessels that feed the tumor. The process of growing new blood vessels is called angiogenesis, and bevacizumab is an angiogenesis inhibitor.

"Bevacizumab blocks the growth factor VEGF, which is important in the process of ovarian cancer progression," says Burger, "and we've seen that

this drug is also active in patients with recurrent disease."

Angiogenesis happens at the interface between the host and the disease, which makes it an appealing target for treatment, says Burger, who also led the Phase II GOG study on using bevacizumab in women with recurrent ovarian cancer. He says different ovarian cancers may appear identical under the microscope but differ biologically, which means they'll respond differently to treatment.

In the *NEJM* paper, Burger and his co-authors point out that another ovarian cancer trial conducted primarily in Europe called ICON7 demonstrated positive results in using becavizumab in combination with chemotherapy and then continued for up to 7 months.

Provided by Fox Chase Cancer Center