

Ovarian cancer outcomes may improve with 'dose-dense' chemotherapy

June 30 2011, By Jeffrey Norris

Dose-dense chemotherapy has shown promise in smaller clinical trials, and now is being investigated in a multi-center, phase III study in which nearly 700 women will participate. Earlier phase II trials pointed to anti-cancer effects for the treatment approach, even when ovarian cancers had become resistant to standard treatment.

The strategy consists of two standard [chemotherapy drugs](#), dosed and timed differently from the current treatment standard. In addition, in the new study women will have the option of receiving a third drug, [bevacizumab](#), which targets [blood-vessel growth](#) in tumors.

Most Deadly Gynecologic Cancer

[Ovarian cancer](#) is the most deadly gynecologic cancer, killing more than 14,000 women yearly. Among cancers that afflict women, breast cancer is the most common and takes the highest toll, but ovarian cancer is more likely to be fatal. The disease often is diagnosed late. Most [new drugs](#) tested in ovarian cancer in recent years have only held cancer at bay for a few months at best.

Only 30 percent to 40 percent of women diagnosed with late-stage ovarian cancer survive five years or more. Most women receive surgery to remove the main tumor mass, followed by chemotherapy.

The aim of the dose-dense treatment is to hit [cancer cells](#) when they are

most vulnerable, killing them before they can give rise to drug-resistant descendants.

The standard chemotherapy includes a taxane drug paclitaxel, combined with a platinum-based drug called [carboplatin](#). Paclitaxel blocks cell division, which leads the targeted cancer cells to commit suicide. However, animal studies showed that the cells stop committing suicide about four days after the standard drug dose is given.

Dose-Dense Protocol

The dose-dense protocol is designed to deprive cancer cells of this window of time for recovery. Lower doses of paclitaxel are given each week, instead of a higher dose every three weeks. Results from earlier clinical studies suggest that this approach may more effectively fight ovarian cancer. A similar dosing strategy for paxlitaxel also has proved beneficial in treating [breast cancer](#), Chan notes.

Women in the study will be randomly assigned to receive either dose-dense treatment or the standard chemotherapy dosing. They will be able to freely choose whether or not to take bevacizumab, which has extended the average time before cancer progresses in Phase III trials. The study is sponsored by the National Institutes of Health through a research cooperative called the Gynecologic Oncology Group.

Doctors will monitor women to track the regrowth of cancer and overall survival, as well as side effects and quality of life.

A treatment design similar to the Phase III protocol formulated by Chan earlier was tested in a major clinical trial in Japan. Half the patients who received dose-dense treatment survived 28 months or longer without their cancers worsening, while the comparable median time to cancer progression in the group that received standard treatment was 17 months.

Based on the results of the Japanese study, the 2011 treatment guidelines for ovarian cancer issued by the National Comprehensive Cancer Network have added dose-dense [paclitaxel](#) as an option for advanced cancers.

Ethnic Differences in Tumor Characteristics

However, according to Chan, ethnic differences in tumor characteristics and treatment responses may be significant. “The Japanese data are promising,” he says, “but the results need to be confirmed in other populations before we change the standard of care throughout the world.”

As part of the study Chan’s clinical research team will be collecting blood samples and tumor specimens to gather information on potential biomarkers that might help predict responses to treatment.

Provided by University of California, San Francisco

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