# CA125 Monitoring Not Beneficial in Ovarian Ca

BY MARY JO M. DALES

ORLANDO — Routine measurements of CA125 conferred no survival advantage in the follow-up of ovarian cancer patients, according to the results of a large, double-blind, prospective, placebo-controlled study presented at the annual meeting of the American Society of Clinical Oncology.

CA125 screening is essential for the diagnosis of ovarian cancer at a stage that is potentially curable. But when used as a monitoring tool for early detection of recurrent cancer in patients in remission, measuring CA125 actually causes women to undergo more cycles of chemotherapy with no improvement in their survival and a decline in their quality of life, reported Dr. Gordon J. Rustin.

This is level 1 evidence that women need not continue to have quarterly measures of CA125 outside the realm of a clinical trial, commented the invited discussant for the paper, Dr. Beth Y. Karlan, a professor of obstetrics and gynecology at the University of California, Los Angeles.

**At 56.9 months of follow-up, women who underwent CA125 monitoring had 'absolutely no difference in survival.'**

DR. RUSTIN

The importance of this study cannot be overemphasized, Dr. Eric P. Winer said during a press briefing at the meeting. These findings can potentially improve the quality of life for all women with stage III or IV ovarian cancer, as well as result in substantial economic savings.

Dr. Rustin, of Mount Vernon Cancer Centre, Middlesex, England, presented the data on behalf of the MRC OV05 (Medical Research Council OV05) and EORTC 55955 (European Organisation for Research and Treatment of Cancer 55955) trial investigators. The trial registered 1,442 patients at 59 sites in 10 countries and was designed to determine whether there were benefits from early treatment of recurrent cancer based on a confirmed elevation of CA125 levels, compared with delaying treatment until clinical symptoms were noted.

Women who had ovarian cancer that was in clinical complete remission after first-line platinum-based chemotherapy and a normal CA125 value were registered in the study. Most were 6 months post diagnosis and had advanced FIGO stage III or IV cancers and serous histology, the type of ovarian cancer expected to relapse. CA125 was measured every 3 months in all of the women. Patients and investigators were blinded to the test results.

CA125 levels exceeded twice the upper limit of normal in 527 patients, who were then randomized to either immediate treatment or to delayed therapy in which they continued to have blinded CA125 measurements but did not begin treatment until they had clinical or symptomatic recurrences. Patients in both arms were treated according to standard local practice. The other 915 patients were not randomized because they had no CA125 rise and no relapse (48%); they relapsed with or without CA125 (30%), they died (6%) or withdrew from the study (14%), or for other reasons (2%).

Patients in the early treatment arm of the study started their regimens 0.8 months after randomization, compared with 5.6 months in the women whose treatment was delayed until they were symptomatic. In the early treatment arm, 68% of women went on to third-line chemotherapy, compared with 56% of women in the delayed treatment arm. Those in the early treatment arm had relapses, on average, 4.6 months earlier than did the women in the delayed treatment arm, an indication that early treatment does not offer longer remissions.

Also, study participants completed quality of life surveys every 3 months. Those in the early treatment arm had earlier declines in quality of life by 3 months. Early chemotherapy not only failed to improve quality of life, it made quality of life worse.

The data were frozen at 56.9 months of follow-up with "absolutely no difference in survival," Dr. Rustin said. The

trial lasted as long as it did because of overall good survival. The study was designed to detect a 10% improvement in 2-year overall survival in the immediate treatment arm.

These findings mean that women can be offered informed choices about CA125 monitoring after first-line chemotherapy, Dr. Rustin said. They can opt to defer testing until they develop symptoms, as long as they recognize the importance of returning at the first sign of symptoms, and feel assured that they will have the same outcomes as women who continue CA125 monitoring.

In the United Kingdom, CA125 tests are available "in the local chemist shop, and women are almost addicted to getting them," he said during an interview. Many say they feel as though they are living from one test to the next. Now they need not have the anxiety that accompanies each routine monitoring test and can rely on clinical symptoms. As a result, these women will have far fewer courses of toxic chemotherapy and the same chance of survival.

Dr. Karlan said the findings will have a major impact on the cost of health care by decreasing the use of resources not shown to improve overall survival and quality of life. There will be less frequent assays, fewer follow-up tests, and improved quality of life.

It will take some time for patients to feel comfortable with this change in approach, she acknowledged, but the message to not worry about the next CA125 value should be a positive one for them. "So many live from one CA125 measure to the next and any small bumps in their levels can cause them great anxiety and distress."

Dr. Karlan commented that the study, although very well done, also has some weaknesses. There was a lack of prescribed secondary- or tertiary-line chemotherapy, and the type of surgery was not considered. New drugs have come along. Platinum resistance and sensitivity were not factored into the analysis.

The study also points out the therapeutic limitations in advanced ovarian cancer, "a choice of whittling away at small disease or carving out large disease." The findings should renew efforts to detect this disease at its earliest, and potentially curable, stage, she said.

The investigators had no relevant conflicts of interest in regard to this study. ■