Changing chemo not beneficial for metastatic B.C. patients with elevated circulating tumor cells

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For women with metastatic breast cancer who had elevated amounts of circulating tumor cells (CTCs) in their blood after a first line of chemotherapy, switching immediately to a different chemotherapy did not improve overall survival or time to progression, according to the results of a phase III clinical trial presented here at the 2013 San Antonio Breast Cancer Symposium, held Dec. 10-14.

"We concluded that CTCs are not a good marker in helping to decide when to switch between chemotherapies," said Jeffrey B. Smerage, M.D., Ph.D., clinical associate professor at the University of Michigan Comprehensive Cancer Center in Ann Arbor. "It had been hoped that switching would both increase the chances of being on an effective therapy and decrease the exposure to toxicity from less effective or ineffective therapies, and as a result it had been hoped that this early switching would result in improved survival and time to progression.

"The most important implication is that we have validated that the group of patients with elevated CTCs at both baseline and 21 days [after starting their first chemotherapy] has a worse prognosis with regard to both time to progression and overall survival," added Smerage. "Although chemotherapy may work for these patients, it clearly does not work as long as one would like. This suggests that this patient population needs more effective treatment options beyond traditional chemotherapy. Given that these patients have higher cancer-related risks,

early consideration of clinical trial participation would be appropriate."

About 75 percent of patients with metastatic breast cancer have CTCs detectable in their blood, and the number of CTCs is elevated in about half of these patients. The presence of elevated CTCs in blood indicates poor prognosis and relatively short time to progression, and the goal of this trial was to evaluate if switching to a different chemotherapy is beneficial for patients whose elevated CTCs did not drop after initial chemotherapy.

This trial found that changing therapy for patients with elevated CTCs after one cycle of initial chemotherapy did not improve their overall survival, the primary endpoint of this study.

"An important secondary endpoint was to evaluate whether the levels of CTCs before and after starting a chemotherapy provided prognostic information on how long a patient might live," Smerage said. "This study confirmed that patients who have low numbers of CTCs before starting chemotherapy have a much better survival. They had a median overall survival of 35 months, which means that half of these patients lived three years or longer, and some substantially longer.

"On the other hand, patients for whom CTCs remained elevated after one cycle of chemotherapy had substantially worse survival. They had a median overall survival of only 13 months," he explained. "This suggests that chemotherapy may not be as effective for these cancers in which CTCs remain elevated after one cycle of chemotherapy. This doesn't mean that chemotherapy has no benefit, but it suggests that the benefit is limited."

Smerage and colleagues conducted a prospective, randomized, phase III trial, called the SWOG S0500 trial, to which they recruited 624 patients between 2006 and 2012. All participants had either measurable disease

or evaluable disease that included bone metastases.

Of the 595 patients who were eligible for the trial, 276 had low CTCs at baseline, and were observed on arm A. These patients continued to receive the initial chemotherapy.

The remaining 319 patients had elevated CTCs at baseline, and 286 had a CTC result available at day 21 of the first cycle of chemotherapy. At day 21, CTCs decreased to lower levels in 163 patients, who were observed on arm B. These patients continued to receive the initial chemotherapy.

The 123 patients who continued to have elevated CTCs at day 21 were either randomly assigned to arm C1 and continued to receive the initial chemotherapy (64 patients) or were randomly assigned to arm C2 and had their treatment changed to a second-line chemotherapy (59 patients).

"This study was based on counting the number of CTCs in blood," said Smerage. "Several groups are now investigating the presence of biological markers such as estrogen receptor, HER2, and others on CTCs. It is hoped that the measurement of these markers may allow for better prediction of what therapies will work best for these patients."

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