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Poor breast cancer prognosis associated with presence of circulating tumor, cancer stem cells

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Metastatic breast cancer patients whose blood contains circulating tumor cells (CTCs) before or after treatment with high-dose chemotherapy and blood stem cell transplant have shorter survival periods, according to a new study by researchers at The University of Texas MD Anderson Cancer Center in Houston.

The findings were presented today in a poster session at the 33rd Annual CTRC-AACR San Antonio Breast Cancer Symposium.

In addition, patients with higher percentages of epithelial cells, or the presence of a specific cellular transition, had higher chances for relapse.

"Building on the information from this study, we eventually may be able to use these molecular markers to identify breast cancer patients with a high likelihood of developing metastasis or relapsing. This may allow physicians to design specific treatments to help patients achieve better outcomes," said James M. Reuben, Ph.D., professor in MD Anderson's Department of Hematopathology, and co-corresponding author of the study.

Stem cells have common receptor

High-dose chemotherapy followed by autologous hematopoietic peripheral blood stem cell transplantation (ASCT) offers modest

complete response rates for some patients with metastatic breast cancer. However, tumor cells that spread to the bone may be recruited and mobilized along with hematopoietic stem cells to increase a patient's chance of relapse.

"We hypothesized that since the breast tumor cells have the same CXRX4 receptor as hematopoietic stem cells, we might mobilize or recruit tumor cells by using a growth factor proven to mobilize blood stem cells," Reuben said.

Epithelial-to-mesenchymal transition (EMT) is recognized as an important part of metastasis. Epithelial cells line the organs and cavities of the body and usually are not mobile. Mesenchymal cells are mobile and can differentiate into many cell types, for example, to repair injury. EMT has been shown to repress E-cadherin, decrease cell-cell adhesion and increase a cell's capacity to move. An estimated 80 percent of solid tumors are cancers of the epithelial tissue.

Blood examined for epithelial cells, CTC

Aphaeresis was used to harvest blood stem cells from 21 metastatic breast cancer patients before transplantation. To determine levels of CTCs, blood samples were collected before aphaeresis (baseline) and one month after transplantation.

"We used the flow cytometry method of staining for both epithelial and stem cell markers," said Hui Gao, Ph.D., a research scientist in MD Anderson's Department of Hematopathology and co-first author of the study. "Then we enumerated the percentages of epithelial cells and cancer stem cells to see how these correlated with patient survival."

Cells, survival correlated

The median time to follow-up after transplant was 16.4 months. At follow-up, eight women were cancer free, and 13 had relapsed. The median time to relapse was nine months, and median survival was 14.4 months.

CTCs were found in six patients before and in nine patients after transplant. Patients with more than five CTCs before transplant had shorter overall survival. If five or more CTCs were found after transplant, both relapse-free and overall survival times were shorter.

Patients with percentages of CD326+ epithelial cells above the median had shorter relapse-free survival times,10 months versus 23 months. Also, patients with CTCs with mesenchymal features had a shorter relapse-free survival, seven months, compared to those who had CTCs without such features, 23 months.

Next steps

The researchers hope to carry the research forward into a prospective study in the near future.

"If we really can target CTCs with mesenchymal features, we may be able to control disease much more efficiently," said Naoto T. Ueno, M.D., Ph.D., professor in MD Anderson's Departments of Breast Medical Oncology and Stem Cell Transplantation and Cellular Therapy, and co-corresponding author of the study.

Provided by University of Texas M. D. Anderson Cancer Center