Neoadjuvant Chemotherapy for Breast Cancer Can Cause Release of Tumor Cells

■ SAN ANTONIO—Using a technique that quantifies circulating tumor cells, German investigators have shown that neoadjuvant chemotherapy with paclitaxel causes a massive release of cells into the circulation, while at the same time reducing the size of the tumor.

Reporting her findings at the 27th Annual San Antonio Breast Cancer Symposium (abstract 6014), Katharina Pachmann, MD, professor of experimental oncology and hematology, Friedrich-Schiller University, Jena, Germany, said that the impact of these released cells on relapse is not clear. The finding could help explain the fact that complete pathologic responses do not correlate well with improvements in survival.

In her study, breast cancer patients undergoing neoadjuvant chemotherapy gave blood samples in which epithelial antigen-positive cells were isolated. Such cells are detected in most breast cancer patients but are rarely found in normal subjects. The investigators measured the levels of circulating tumor cells before and during primary chemotherapy with several different cytotoxic agents.

"During the applied combination therapy, three different phases could be observed," she said. "An initial decline in the number of circulating cells during the epirubicin (Ellence)-containing part of the regimen, followed by a steep increase during paclitaxel treatment, and a subsequent re-decrease if a third segment with CMF (cyclophosphamide/methotrexate/fluorouracil) was administered before surgery."

Ironically, she said, paclitaxel produces the greatest degree of tumor shrinkage but also the greatest release of circulating tumor cells. In three different paclitaxel-containing regimens, with five to eight patients in each group, circulating cell numbers massively increased whereas tumor size decreased. These cells remained in the circulation for at least 5 months after surgery, Dr. Pachmann reported.

"The tumor collapses, but we find more cells in the circulation. This corresponds with a high pathologic complete response during paclitaxel treatment, but in the end, this is not reflected in improved survival," she said. "These cells are alive in the circulation, and they would be accessible to an additional treatment, such as tamoxifen. We have shown that tamoxifen treatment will reduce circulating tumor cells in some patients but not all. In this study, the patients received no further treatment after surgery."

She noted that the initial decrease in circulating tumor cells correctly predicted final tumor reduction in patients with HER2-negative tumors, but this correlation was less pronounced in HER2-positive patients who additionally received trastuzumab (Herceptin).

At this point, the implications of these findings are unclear. "The results indicate, at least, that monitoring of circulating tumor cells can contribute to our understanding of tumor/blood interactions and may provide a valuable tool for therapy monitoring in solid tumors," Dr. Pachmann said. ONI

[**DR. PACHMANN: To illustrate this article, can you provide a photo of isolated cells and the graph from your poster showing increase/decrease in cells via different regimens?**

If so, please send electronically to JSkinner@cmp.com. Please provide in high-resolution (300 dpi if possible) tiff or jpg format if possible, although sometimes we can use powerpoint images. Thanks, June.]