Surgery and radiation do not extend survival in newly diagnosed metastatic breast cancer

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Up to now, women who present with a new diagnosis of breast cancer that is already in an advanced stage (stage IV) face an unanswered question about whether surgery and radiation to the tumor in the breast (local therapy) will prolong survival compared to the traditional treatment of systemic treatment alone. Data from the long-awaited E2108 randomized phase three trial show that the survival experience of the two treatments was the same; local therapy did not improve overall survival. The goal of the E2108 study was to determine whether surgery and radiation should become routine practice for patients with stage IV breast cancer and resolve conflicting data from two earlier randomized trials.

The American Society of Clinical Oncology (ASCO) will highlight the data during the plenary session of its annual meeting to occur virtually from May 29-31 (Abstract LBA2). The ECOG-ACRIN Cancer Research Group (ECOG-ACRIN) designed and led this trial, which was conducted in the NCI National Clinical Trials Network (NCTN) with funding from the National Cancer Institute, part of the National Institutes of Health.

"Based on the results of our study, women who present with a new diagnosis of breast cancer already in stage IV should not be offered surgery and radiation for the primary breast tumor with the expectation of a survival benefit," said lead investigator Seema A Khan, MD (Northwestern University). "When making these decisions, it is important to focus energy and resources on proven therapies that can prolong life."

About one in every 20 women diagnosed with breast cancer in the United States each year present with cancer that has already spread beyond the breast to other organs (also called stage IV, advanced, metastatic, or distant breast cancer). Patients with stage IV breast cancer usually receive systemic treatment—drugs that travel through the bloodstream and treat disease throughout the body. Examples of systemic treatments are: chemotherapy to attack cells that grow quickly, targeted therapy that attacks specific proteins on cancer cells, hormonal therapy that either blocks or decreases the level of the body's natural hormones, which sometimes act to promote cancer growth, and, immunotherapy to stimulate the patient's immune system to attack the cancer.

Traditionally, it was thought that because metastases had occurred, local therapy would not provide any additional survival benefit beyond what systemic treatment could offer. Starting about 20 years ago, this approach was questioned based on the idea that the primary tumor could be a source of re-seeding of cancer outside the breast. Several studies suggested that removal of the tumor in the breast with surgery would be beneficial. However, these studies were flawed because women receiving surgery tended to be younger, healthier, and have less severe disease. It became clear that a clinical trial was needed to provide women and their doctors with good information. Further complicating matters, two randomized clinical trials published in the last five years had conflicting results.

In E2108, 390 women with stage IV breast cancer were enrolled. All received the optimal systemic treatment for them based on the number of other organ systems involved and tumor biomarker status. Of those whose disease responded to initial systemic therapy, or stayed stable, 256 women agreed to be randomized to either continue with systemic therapy or to receive surgery and radiation (local therapy) and then continue on with systemic treatment.

The main goal of the E2108 trial was to see if the use of local therapy to the breast tumor would improve survival. The results show that the survival experience of the two groups was identical (half of them alive after 4.5 years).
"When combined with the results of an earlier trial in Mumbai, India (Badwe et al, Lancet Oncol 2015), these results tip the scales against the possibility that local therapy to the breast tumor will help women live longer," said Dr. Khan. "The Indian trial had a similar design to E2108, and also showed similar results between the two treatment groups."

The E2108 trial also compared patient-reported quality of life (depression, anxiety, and well-being for example) between the two groups. It found that there was no quality of life advantage in the group of women who received local therapy to the breast tumor.

"This result was a little surprising since one of the reasons for considering surgery and radiation is the idea that growth of the tumor will impair quality of life," said Dr. Khan. "Instead, we find that the adverse effects of surgery and radiation appear to balance out the gains in quality of life that were achieved with better control of the primary tumor."

"ECOG-ACRIN also conducted TAILORx to help women and their physicians avoid unnecessary chemotherapy treatment and its toxicity for those diagnosed with early stage, hormone receptor positive disease," said ECOG-ACRIN Breast Cancer Committee Chair Antonio C. Wolff, MD (Johns Hopkins University). "Trials like TAILORx, and now E2108, help ECOG-ACRIN, in a partnership with the National Cancer Institute and investigators all over the world, fulfill our mission to identify the best treatments for an individual patient and maximize quality of life."

Provided by ECOG-ACRIN Cancer Research Group


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