MedicalXpress

Adjuvant chemo might not add benefit in breast cancer patients who have excellent response to neoadjuvant chemo

December 5 2018

Pathological complete response (pCR) after neoadjuvant (presurgery) chemotherapy was associated with significantly lower recurrence risk and higher overall survival in breast cancer patients, and pCR after neoadjuvant chemotherapy had similar association with improved outcomes among those who received additional chemotherapy following surgery (adjuvant chemotherapy) versus those who did not, according to meta-analyses of data from 52 clinical trials, presented at the 2018 San Antonio Breast Cancer Symposium, held Dec. 4-8.

A pCR was defined as the lack of all signs of invasive cancer in the breast tissue and lymph nodes removed during surgery after treatment with chemotherapy.

"The focus of many breast cancer trials for several years has been on adding additional systemic therapies to reduce recurrence risk; however, adding therapies also leads to additional toxicity and overtreatment for many women," said Laura Spring, MD, medical oncologist at Massachusetts General Hospital Cancer Center and instructor in medicine at Harvard Medical School.

Spring and colleagues conducted a comprehensive patient-level meta-analysis of studies on neoadjuvant chemotherapy for localized breast cancer to evaluate the potential association between pCR after neoadjuvant therapy and subsequent breast cancer recurrence, and to

evaluate the impact of adjuvant chemotherapy in modulating the relationship between pCR and outcomes.

"We demonstrated that pCR was strongly associated with higher event-free and overall survival, and the association was similar among those who received additional adjuvant cytotoxic chemotherapy after surgery versus those who did not," Dr. Spring said.

"Overall the study findings from our team support the concept of therapeutic escalation/de-escalation strategies in the adjuvant setting based on initial neoadjuvant response, and highlight the need for additional research to personalize the "right" amount of therapy for patient with breast cancer," noted Aditya Bardia, MD, MPH, senior author and director of Precision Medicine at Center for Breast Cancer, Massachusetts General Hospital, Harvard Medical School.

The team conducted a PubMed search and identified eligible clinical trials from 1999 to 2016. Of the 3,209 abstracts reviewed, 27,895 patients from 52 studies met inclusion criteria. A variety of treatments were used in these studies. "To account for treatment differences in our statistical approach, we used a random effects model, which is more conservative than other approaches, and also performed a number of sensitivity analyses to confirm results," Spring noted.

Overall, breast cancer patients who had a pCR were 69 percent less likely to have disease recurrence compared with those who did not have a pCR. The relationship was strongest among patients with triple-negative or HER2+ breast cancer with a pCR, where such patients were 82 percent and 68 percent less likely, respectively, to have disease recurrence.

Patients with hormone receptor (HR)-positive breast cancer who had a pCR had a trend toward lower risk for recurrence compared with those

without a pCR, but the data were not statistically significant. "Other research, such as from the I-SPY2 trial and the FDA-led meta-analysis of pCR, has demonstrated that there is a significant relationship between pCR and long-term outcomes for high-grade HR+ tumors and much less so for low-grade HR+ tumors. For HR+ breast cancer, an alternative surrogate endpoint such as the residual cancer burden (RCB) index may be more appropriate as pCR rates are low overall in this population," Spring said.

Breast cancer patients with a pCR also had a 78 percent lower risk for mortality compared with those who did not have pCR overall, and similar trends were seen among the three major clinical subtypes of breast cancer.

Notably, the association of pCR with reduced recurrence was comparable between patients who received adjuvant chemotherapy (66 percent less likely to have recurrence) and those who did not receive adjuvant chemotherapy (64 percent less likely to have recurrence).

"The finding possibly reflects tumor biology, wherein tumors sensitive to neoadjuvant therapy in breast and lymph nodes are also typically sensitive to the therapy in micrometastatic sites," Spring explained. "Presence of complete response in breast and axilla is likely associated with complete response in micrometastatic sites, minimizing the added benefit from additional adjuvant therapy. A notable exception may be therapy sanctuary sites, such as the central nervous system."

The team added, "We also created a statistical model to demonstrate the relationship between the magnitude of pCR change and corresponding change in event-free and overall survival. The statistical model will hopefully provide useful guidance for clinical trials evaluating neoadjuvant therapies for patients with localized breast cancer."

A main limitation of the study is that the analysis was subject to variable reporting and study-specific outcome definitions used across studies. "Also, this was not a randomized trial, and there was heterogeneity in the type of neoadjuvant therapies employed and the study results are broadly based on neoadjuvant chemotherapy in general rather than a specific therapeutic regimen," Spring added.

Provided by American Association for Cancer Research