Increasing the dose intensity of chemotherapy may lower the risk of breast cancer recurrence and death

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Increasing the dose intensity of chemotherapy by either shortening the intervals between the cycles or by sequential administration instead of concurrent administration of the drugs reduced the risk of early-stage breast cancer recurrence and death compared with standard chemotherapy regimens, according to data from an EBCTCG meta-analysis study presented at the 2017 San Antonio Breast Cancer Symposium, held Dec. 5–9.

"The number of deaths from breast cancer in the United States and many other countries has halved over the last 30 years because of a series of step-by-step improvements in treatment that, together, add up to make a big difference," said Richard Gray, MSc, professor of medical statistics in the Nuffield Department of Population Health at University of Oxford, United Kingdom. "It is important to continue to find out whether or not there are worthwhile benefits from one treatment compared to another."

Gray and colleagues aimed to find out whether increasing the dose intensity of chemotherapy, meaning increasing the amount of drug delivered per unit time, was more effective at lowering breast cancer recurrence and death rates than standard chemotherapy regimens for patients with early-stage breast cancer. The dose-dense chemotherapy trials used the same chemotherapy agents at the same doses but administered every two weeks instead of every three weeks. The average

weekly dose is therefore 1.5 times higher in the dose-dense group than with the standard schedule comparator, Gray explained.

"Another way of increasing the dose intensity of chemotherapy is to give the chemotherapeutics individually in sequence rather than administering all the drugs together at the same time," said Gray. This sequential approach allows higher doses of the individual drugs to be used in each cycle while keeping the side effects manageable, he added.

For the meta-analysis, Gray and team used individual patient data from seven randomized trials (10,004 women) that tested chemotherapy given every two weeks versus every three weeks, and from nine randomized trials (11,533 women) that tested sequential versus concurrent anthracycline and taxane-based chemotherapies.

"We were surprised by how strong and consistent the findings from our study were," Gray said.

Patients who received chemotherapy every two weeks were 17 percent and 15 percent less likely to have disease recurrence and die from breast cancer within 10 years, respectively, compared with those who received treatment every three weeks.

Similarly, patients who received sequential chemotherapy were 14 percent and 13 percent less likely to have disease recurrence and die from breast cancer within 10 years, respectively, compared with those who received concurrent treatment.

"The results apply to most women receiving chemotherapy for early-stage breast cancer: the 15 percent reduction in recurrence with dose-intense chemotherapy across all trials was similar in ER-positive and in ER-negative disease, and did not differ significantly by any other patient or tumor characteristics, including age, HER2 status, nodal status, tumor

size, and grade," noted Gray.

There were few additional side-effects with dose-intense schedule compared with standard schedule chemotherapy, and fewer patients who received dose-intense treatment died from non-breast cancer causes than those who received standard treatment.

"Some centers prefer giving chemotherapy every three weeks and offer treatment every two weeks less frequently because of concerns about side effects and uncertainty about the additional benefit. Looking at the data from large numbers of women receiving dose-intense chemotherapy, we have found no evidence to justify these concerns, and the results show consistent benefit from the more intense treatments," Gray said.

A limitation of the study is that the chemotherapy used in the dose-intensification trials varied in the doses, the number of treatment cycles, and the agents used. So, although dose-intense chemotherapy is clearly more effective at eradicating cancers, it is difficult to recommend any one particular dose-intense chemotherapy regimen based on this study, said Gray.

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