Adjuvant capecitabine did not improve outcomes for patients with early triple-negative breast cancer

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Treating patients who had early-stage triple-negative breast cancer with the chemotherapy agent capecitabine after they completed surgery and standard chemotherapy did not significantly improve disease-free or overall survival compared with observation, according to data from the randomized, phase III GEICAM/CIBOMA clinical trial presented at the 2018 San Antonio Breast Cancer Symposium, held Dec. 4-8.

"Patients with early-stage triple-negative breast cancer are usually treated with surgery and chemotherapy, and sometimes radiotherapy," said Miguel Martín, MD, Ph.D., professor of medicine and head of the Medical Oncology Service at Hospital Gregorio Marañón, Universidad Complutense, Madrid, Spain. "New therapeutic approaches are urgently needed, however, because the risk of relapse is high: 7 to 10 percent of those with stage 1 disease relapse, 15 to 20 percent of those with stage II disease, and 25 to 50 percent of those with stage III disease.

"We were disappointed to find that adding adjuvant capecitabine to the standard treatment did not significantly improve disease-free or overall survival," continued Martín. "However, given that we found a subset of the patients with nonbasal-like disease seemed to have a significant benefit from capecitabine, and data from the CREATE-X trial showed that adjuvant capecitabine significantly reduced the rate of relapse and improved overall survival when administered to breast cancer patients with residual disease after neoadjuvant chemotherapy, we strongly

recommend that patients with triple-negative breast cancer discuss adjuvant capecitabine with their oncologists."

Martín and colleagues randomized 876 patients with early-stage triple-negative breast cancer who had been treated with surgery and chemotherapy in the trial to eight cycles of capecitabine or observation.

After a median follow-up of 7.3 years, five-year disease-free survival was 79.6 percent among the 448 patients randomized to capecitabine and 76.8 percent among the 428 patients randomized to observation. The improvement in five-year disease-free survival was not statistically significant, meaning that the trial result is formally negative, explained Martín.

"There was a nonsignificant trend in favor of capecitabine, but the trial had only 876 participants, which means it was not statistically powered to identify small but clinically relevant differences," noted Martín. "One possible reason for the discrepancy in the results of the CREATE-X trial and our trial may be that the populations had different prognostic features; the risk of relapse of our population was much less than in the CREATE-X trial."

In subgroup analyses, Martín and colleagues found that among the 248 patients with nonbasal-like disease, as defined by immunohistochemistry, those randomized to adjuvant capecitabine were 49 percent less likely to experience a disease event and 52 percent less likely to die compared with those randomized to observation.

"This is an intriguing finding," said Martín. "However, it should be interpreted with caution because the interaction test was negative for disease-free survival (p=0.0694), although it was statistically significant for overall survival (p=0.0052)."

According to Martín, the main limitation of the study is the limited power of the trial to show small but clinically relevant improvements in outcome with capecitabine due to the sample size and the lower than expected number of relapse events in the control arm.

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