Landmark study confirms chemotherapy benefit in breast cancer patients

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Chemotherapy generally improves survival in postmenopausal breast cancer patients, according to a landmark study led by Dr. Kathy Albain of Loyola University Health System.

However a second study, also headed by Albain, found that a multigene test on a breast tumor can identify a subset of women who may not benefit from chemotherapy.

The related studies were published simultaneously online, ahead of print, Dec. 10 in the journals Lancet and *Lancet Oncology*.

"With the right chemotherapy regimen, we can favorably impact survival," Albain said. "But it also is important to avoid the toxicity and medical costs of chemotherapy when it may not be needed."

Tamoxifen has long been a standard drug treatment for postmenopausal women with the most common type of breast cancer, known as estrogen-receptor positive. Tamoxifen blocks estrogen's linkage with cancer cells, thus preventing the hormone from promoting cancer cells' growth.

There has been much debate over whether women with tumors that are fueled by estrogen would benefit from receiving chemotherapy drugs in addition to standard antihormonal treatments such as tamoxifen. Previous studies found little or no benefit from adding chemotherapy in postmenopausal patients.

The new study is considered groundbreaking because it is more definitive than past studies and because it has set the current standard of care. The study was conducted by the Southwest Oncology Group, one of the largest federally funded clinical trial networks, and was funded by the National Cancer Institute.

The study followed a homogenous population of 1,477 women from multiple centers for 10 years. Unlike earlier studies, it included a regimen of anthracycline chemotherapy and a tamoxifen-alone control group.

The women were postmenopausal, and had hormone receptor-positive cancer that had spread to at least one lymph node in the armpit area. Women who received chemotherapy were 24 percent less likely to see their cancer come back. They also were 17 percent less likely to die during the time period they were followed, but this finding fell just short of being statistically significant.

All women in the study took a tamoxifen pill every day for five years. Researchers randomly assigned 361 patients to receive tamoxifen alone and 1,116 patients to receive tamoxifen plus a three-drug chemotherapy regimen for six months.

The chemotherapy regimen is known as CAF (cyclophosphamide, Adriamycin® and 5-fluorouracil). Women who underwent chemotherapy were more likely to experience a drop in infection-fighting white blood cells, soreness and painful ulcers in the mouth, blood clots, congestive heart failure and leukemia than those who received tamoxifen alone.

The study established the standard of care regarding when to give tamoxifen in relation to chemotherapy. The chemotherapy group was divided into women who began taking tamoxifen during chemotherapy

and those who waited until they were done with chemotherapy before taking tamoxifen. Women who took tamoxifen after chemotherapy had better disease-free survival and overall survival.

Over the past several years, Albain and colleagues have presented ongoing data from this study, and their findings already have influenced how doctors around the world are treating breast cancer.

In the second study, published in *Lancet Oncology*, Albain and colleagues did a retrospective analysis to determine whether a 21-gene test can predict which women would benefit from chemotherapy.

The test, Oncotype DX®, is performed by Genomic Health Inc. The test examines 21 genes from a tumor sample to determine how active they are. A score is reported, which is then correlated with benefit to chemotherapy. The analysis found there appeared to be no benefit to women who had a low score on the gene test, while those with higher scores did benefit.

More than 100,000 breast cancer patients have undergone the test since it became commercially available in 2004 for patients with estrogen-receptor positive breast cancer that has not spread to the lymph nodes. The new study indicates the test also could be useful in predicting whether chemotherapy -- the current standard -- could be avoided in a subgroup of patients whose cancer has spread to lymph nodes, Albain said.

"This study, along with other studies involving different gene tests, suggests that certain biologic subtypes of breast cancer may inherently be either susceptible to chemotherapy or resistant to chemotherapy," Albain said. "Prospective studies with larger sample sizes are needed to determine who will optimally benefit from chemotherapy."

Source: Loyola University Health System (news : web)