Exemestane may be another first-line, adjuvant therapy for hormone-receptor positive, early-stage breast cancer

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Exemestane, an aromatase inhibitor that blocks production of estrogen, may provide another post-surgery option for postmenopausal women with hormone-receptor positive, early-stage breast cancer.

In the first head-to-head adjuvant clinical trial comparing two aromatase inhibitors, anastrozole and exemestane, the drugs resulted in similar survival rates and prevention of breast cancer recurrences. Some differences in the side effect profile were seen, including a potential difference in the risk of developing osteoporosis.

Paul E. Goss, M.D., Ph.D., professor of medicine at Harvard Medical School in Boston, presented detailed results of this study at the 33rd Annual CTRC-AACR San Antonio Breast Cancer Symposium, held Dec. 8-12, 2010.

In hormone-receptor positive breast cancer estrogen stimulates tumor growth. Currently, patients undergo surgery and then receive drugs that stop estrogen production for five years. Aromatase inhibitors block an enzyme, which is responsible for converting androgens to estrogens.

In previous research, aromatase inhibitors have shown superiority over standard endocrine therapies, with anastrozole and letrozole as the only drugs in the class approved by the U.S. Food and Drug Administration (FDA) as a first-line, adjuvant therapy.

But Goss said investigators had hypothesized that another class of aromatase inhibitors, of which exemestane is an example, may be more potent and have a more favorable side effect profile, including less damage to bones, organs and lipid metabolism.

"The difference in the drug class is that anastrozole is a non-steroidal inhibitor and exemestane is a steroidal inhibitor," said Goss.

To test this hypothesis, the NCIC Clinical Trials Group at Queen's University, Canada, led a large, randomized clinical trial comparing the two treatments among 7,576 women from Canada, the United States and Europe. The trial included support from the U.S. National Cancer Institute's Cancer Therapy Evaluation Program and the European-based International Breast Cancer Study Group.

"We found that the drugs are comparable in terms of preventing recurrent breast cancer and in overall survival," said Goss. "Osteoporosis was reported less frequently and cholesterol levels appeared to be lower in patients on exemestane than anastrozole. Other side effects such as mood change and abnormalities of blood tests assessing liver function were reported more frequently with exemestane, although, the overall numbers of these events were small. With these results, exemestane should be considered as an alternative to anastrozole for initial adjuvant therapy."

Exemestane is currently approved by the FDA when used following tamoxifen, a standard endocrine therapy, or as a second-line therapy for metastatic breast cancer.

"The three available aromatase inhibitors are due to come off patent and these results provide another alternative for the most commonly prescribed medication for breast cancer globally," he said.

The good news for patients is how well women in this trial did, with a reported 91 percent overall survival rate after more than four years of follow-up, according to Goss. "The results are likely as a result of a combination of many advances including screening, surgery, radiation, chemotherapy and endocrine therapy," he said.

Initially, the researcher's clinical trial also included investigating the role of a COX-2 inhibitor called celecoxib when used in combination with the aromatase inhibitors. Less than two years into this seven-year trial, this portion of the study was discontinued because of concerns about heart problems associated with COX-2 inhibitors. A total of 1,635 women had received celecoxib at that time.

COX-2 inhibitors are nonsteroidal anti-inflammatory drugs that reduce inflammation by blocking COX-2 enzyme, which is responsible for the pain and swelling associated with inflammation. They are also produced in response to precancerous and cancerous tissues.

"Therefore, the value of COX-2 inhibitors in reducing breast cancer recurrence remains unanswered," said Goss.

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