Presurgery abemaciclib treatment reduces cell proliferation in (HR)-positive, HER2-negative breast cancer

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Presurgery treatment with the investigational therapeutic abemaciclib, either alone or in combination with the aromatase inhibitor anastrozole, reduced levels of Ki67, a marker of cell proliferation, in hormone receptor (HR)-positive, HER2-negative breast cancer cells, compared with anastrozole alone, according to data from the neoMONARCH phase II clinical trial presented at the 2016 San Antonio Breast Cancer Symposium, held Dec. 6–10.

"Anticancer therapeutics that target CDK4 and CDK6 have largely been studied as treatments for advanced HR-positive, HER2-negative breast cancer, with one such drug, palbociclib (Ibrance), approved for use in this setting," said Sara A. Hurvitz, MD, associate professor of medicine at the University of California, Los Angeles (UCLA), and medical director of UCLA's Jonsson Comprehensive Cancer Center Clinical Research Unit. "We set out to investigate whether the CDK4 and CDK6 inhibitor abemaciclib would have measurable biological effects on early-stage HR-positive, HER2-negative breast cancer.

"We found that abemaciclib reduced levels of Ki67 in HR-positive, HER2-negative breast cancer cells," continued Hurvitz. "Reduced Ki67 levels, which indicate reduced cell proliferation, have been shown in other studies to correlate with improved outcomes. Therefore, our data suggest that CDK4/6 inhibitors may benefit patients with early-stage disease. More definitive clinical evaluation of these therapeutics in the

early-stage setting should be a priority."

Hurvitz explained that treatment before surgery, which is called neoadjuvant therapy, aims to reduce the size of the tumor and eradicate any cells that may have spread beyond the breast. For patients with early-stage HR-positive, HER2-negative breast cancer, neoadjuvant therapy usually consists of chemotherapy or endocrine therapy, she said.

The researchers randomly assigned 223 postmenopausal women with early-stage HR-positive, HER2-negative breast cancer to neoadjuvant therapy with anastrozole, abemaciclib, or anastrozole plus abemaciclib for two weeks. All patients then received anastrozole plus abemaciclib for 14 weeks, at which point they had surgery. To assess the primary outcome measure of change in Ki67 levels from baseline to two weeks, core biopsies taken before and after the first two weeks of treatment were analyzed for Ki67.

The study met its primary endpoint by showing that Ki67 levels were significantly reduced in breast cancer cells from the 107 patients who received abemaciclib, either alone or in combination with anastrozole, compared with the 54 patients who received anastrozole only.

Treatment with abemaciclib plus anastrozole led to a reduction in tumor size in most patients, as assessed by clinical and radiological evaluation.

"Even though the results of this study were positive and promising, they will not change the standard of care because this was a proof of concept study," said Hurvitz. "The duration of therapy was relatively short and did not allow us to robustly assess pathologic responses, nor were we able to follow patients to evaluate long-term outcome. Nonetheless, the data generated are important and support continued evaluation of this drug in early-stage breast cancer."