Palbociclib showed antiproliferative activity in early-stage breast cancer

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The molecularly targeted therapeutic palbociclib (Ibrance), which is used to treat advanced breast cancer, was effective in slowing the multiplication of cancer cells in patients diagnosed with early-stage breast cancer who received no prior therapy, according to data from a phase II clinical trial presented here at the AACR Annual Meeting 2016, April 16-20.

"The use of targeted therapies has been increasing in the last few years. It is crucial to determine that these drugs do hold activity against tumor cells," said the study's lead author, Monica Arnedos, MD, an assistant professor at Gustave Roussy Cancer Campus in Villejuif, France. "In the case of palbociclib, no predictive biomarkers have been identified to date, and there are still no data about its potential efficacy in the early setting."

Palbociclib, an inhibitor of cyclin-dependent kinases (CDK) 4 and 6, was approved by the U.S. Food and Drug Administration (FDA) in February 2015 for use in combination with the anti-estrogen therapeutic letrozole for treating postmenopausal women with a specific subtype of breast cancer: estrogen receptor-positive, HER2-negative, metastatic breast cancer.

In this clinical trial, Arnedos and colleagues sought to determine whether short-term preoperative palbociclib treatment was associated with decreased cancer cell proliferation and other biomarker changes in the tumors of patients with different subtypes of early-stage breast cancer.

This randomized study included 100 women who had been diagnosed with early-stage breast cancer. Seventy-four received 125 mg of oral palbociclib daily for 14 days leading up to breast cancer surgery. The 26 patients in the control arm received no treatment. Overall, 93 percent of the tumors were hormone receptor-positive (HR+)/HER2-negative (HER2-) and 8 percent were HER2-positive. Tissue samples were extracted at baseline and at surgery.

The study found that 58 percent of patients who had received palbociclib had an antiproliferative response in their tumors, compared with 10 percent of those in the control group.

Specifically, the researchers found that the protein Ki67, which is a marker of cell proliferation, decreased in the tumors of patients treated with palbociclib. The change was most significant in patients with HR+/HER2- breast cancer. In that group, 72 percent of patients showed decreased Ki67, compared with 5 percent of the patients in the control group. Arnedos noted that no Ki67 response was observed in women with HER2-positive tumors or triple-negative breast cancer. However, she noted that a limitation of the study is that there weren't enough patients with HR-negative breast cancer, which made it difficult to interpret the findings for that group.

Arnedos plans to discuss the effect of palbociclib on several other biomarkers at the meeting, including PIK3CA, an oncogene that is commonly mutated in certain subtypes of breast cancer.

Although further research will be necessary to confirm the findings of this study, Arnedos said the results were promising for a new body of patients.

"Palbociclib works in untreated early-stage breast cancer, and the magnitude of this activity was higher than expected," Arnedos said.