# FDA Approves New Targeted Therapy for Advanced Breast Cancer

Piqray plus Faslodex prolonged progression-free survival for metastatic breast cancer patients with PIK3CA gene mutation.

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The Food and Drug Administration (FDA) has approved the PI3K inhibitor Piqray (alpelisib) in combination with Faslodex (fulvestrant) for postmenopausal women, and men, with previously treated hormone receptor-positive, HER2-negative advanced or metastatic breast cancer with PIK3CA mutations. The agency also approved a new diagnostic test to identify patients who could potentially benefit from this treatment.

Approval was based on findings from the Phase III SOLAR-1 trial, which showed that the combination improved progression-free survival (PFS) by 35% compared with Faslodex alone and led to tumor shrinkage in about a third of study participants.

“Today’s approval is expected to change the way we practice medicine in advanced breast cancer. For the first time, physicians can test for PIK3CA biomarkers and develop a treatment plan based on the genomic profile of a patient’s cancer,” lead investigator Fabrice André, MD, PhD, of Institut Gustave Roussy near Paris said in a Novartis press release. “In the SOLAR-1 Phase III trial, alpelisib plus fulvestrant nearly doubled median PFS and more than doubled overall response rate in patients with a PIK3CA mutation, offering them new hope for longer life without progression.”

Piqray inhibits phosphatidylinositol-3-kinase (PI3K), an enzyme that plays a role in cell growth and metabolism. It works against cancer with mutations in the PIK3CA gene, which occur in about 40% of hormone receptor-positive advanced breast tumors. Unlike earlier drugs in its class (some of which are approved for leukemia and lymphoma), Piqray has more specific activity against the alpha isoform of PI3K, which leads to fewer side effects. It is taken as two tablets once daily with food.

The SOLAR-1 study compared Piqray plus Faslodex (an estrogen receptor blocker) versus Faslodex alone in postmenopausal women and a small number of men who had hormone receptor-positive, HER2-negative advanced or metastatic breast cancer.

Breast cancer is classified by the type of receptors it expresses. A majority of breast cancers are hormone receptor-positive (HR-positive), meaning they carry receptors for estrogen or

progesterone; treatment usually includes hormone therapy. About 20% of tumors overexpress HER2 (human epidermal growth factor receptor 2) and can be treated with HER2 inhibitors like Herceptin (trastuzumab). Triple-negative breast cancer carries none of these receptors and is harder to treat.

Study participants had previously used an aromatase inhibitor (a drug that prevents the conversion of other hormones to estrogen) and could also have tried an additional prior line of treatment, including CDK4/6 inhibitors such as Ibrance (palbociclib), Kisqali (ribociclib) or Verzenio (abemaciclib).

As reported at the San Antonio Breast Cancer Symposium in December, people with PIK3CA mutations who were assigned to take Piqray plus Faslodex had a median progression-free survival duration—meaning they were still alive without worsening of disease—of 11.0 month compared with 5.7 months for those treated with Faslodex alone. Overall survival results were immature, but showed a trend towards improvement with Piqray. The overall response rate—meaning complete or partial tumor shrinkage—was 36% in the Piqray combination group compared with 16% in the Faslodex-only group.

Looking at treatment history, people who had tried a second line of prior therapy saw a greater benefit from adding Piqray. The risk of disease progression or death fell by 29% among patients treated with only an aromatase inhibitor, but by 39% among those who had also used any prior second-line therapy and by 52% among those who previously used a CDK4/6 inhibitor. Piqray showed no benefit, however, in another study cohort of people without PIK3CA mutations.

The Piqray combination was generally safe but caused more side effects than Faslodex alone. However, just 3% of people treated with the Piqray regimen and 2% in the Faslodex-only group permanently stopped treatment because of side effects.

Common side effects of Piqray include diarrhea, nausea, weight loss, rash, fatigue, mouth sores, decreased appetite, hair loss, low white blood cell count and various laboratory abnormalities including high blood sugar and elevated liver enzymes. More serious side effects may include severe hypersensitivity reactions, severe skin rash, severe diarrhea and serious hyperglycemia. Piqray can cause fetal harm if used during pregnancy.

“Piqray is the first PI3K inhibitor to demonstrate a clinically meaningful benefit in treating patients with this type of breast cancer,” Richard Pazdur, MD, director of the FDA’s Oncology Center of Excellence, said in a press release. “The ability to target treatment to a patient’s specific genetic mutation or biomarker is becoming increasingly common in cancer treatment, and companion diagnostic tests assist oncologists in selecting patients who may benefit from these targeted treatments.”

Pazdur noted that Piqray is the first novel drug to be approved under the FDA’s Real-Time Oncology Review pilot program, which aims to speed up approval of new treatments that address

unmet medical needs.

“If you are facing a complex disease like metastatic breast cancer, you want to follow a path that is specific to your type of disease,” said Shirley Mertz of the Metastatic Breast Cancer Network. “Finding the right treatment team and getting the right tests, like testing for the PIK3CA mutation, will help your healthcare team identify accurate, precise treatment options for your disease.”

Click here to read a Novartis press release about the approval.

Click here for full prescribing information for Piqray.

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