Ibrance Slows Progression of Double-Positive Metastatic Breast Cancer

Addition of the CDK 4/6 inhibitor improved progression-free survival by 15.2 months for patients with HR-positive/HER2-positive advanced breast cancer.

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When added to standard first-line maintenance therapy, Ibrance (palbociclib) delayed disease progression in people with advanced hormone receptor-positive/HER2-positive breast cancer, according to results from the PATINA trial presented at the San Antonio Breast Cancer Symposium (SABCS 2024).

“PATINA is the first large Phase III study to show the benefit of CDK4/6 inhibition in HR-positive, HER2-positive metastatic breast cancer,” principal investigator Otto Metzger, MD, of the Dana-Farber Cancer Institute, said in a news release. “These results support the potential of this maintenance treatment to slow disease progression and improve clinical outcomes in this patient population.”

Breast cancer is classified by the types of receptors it expresses. Most breast tumors carry receptors for the hormones estrogen and/or progesterone (known as HR-positive), which spur cancer growth, and they can be treated with endocrine therapy. About 15% of tumors express human epidermal growth factor receptor 2 (HER2), making them susceptible to HER2-blocking drugs such as Herceptin (trastuzumab) and Perjeta (pertuzumab). Triple-negative breast cancer doesn’t express any of these receptors and is more difficult to treat.

Ibrance is a cyclindependent kinase inhibitor that blocks both CDK4 and CDK6, proteins that play a role in regulating cell division. Ibrance was initially approved in 2015 for women with locally advanced or metastatic HR-positive/HER2-negative breast cancer, which is by far the most common type; this indication was later expanded to include men. The new data show that the medication also works for patients with HR-positive/HER2-positive tumors—dubbed “double-positive”—which account for around 10% of all cases.

Based on preclinical evidence showing that CDK4/6 inhibitors appear to help prevent resistance to endocrine therapy and HER2 blockers, the PATINA trial was designed to test the safety and effectiveness of adding Ibrance to standard hormone and anti-HER2 maintenance therapy for people with double-positive metastatic breast cancer.

This open-label study enrolled 518 patients in eight countries with HR-positive/HER2-positive breast tumors. Almost all were women, the median age was 53 years and more than 90% were white.

The participants first received six to eight cycles of induction chemotherapy plus Herceptin, with or without Perjeta, and had no evidence of disease progression. They were then randomly assigned to receive first-line maintenance therapy using Ibrance plus HER2 inhibitors and endocrine therapy or anti-HER2 and endocrine therapy alone. Endocrine therapy options included an aromatase inhibitor (a drug that blocks an enzyme that converts androgens to estrogen) or Faslodex (fulvestrant); premenopausal women used medications to suppress hormone production by the ovaries. Almost all used both HER2 inhibitors, and more than 90% used an aromatase inhibitor. Treatment continued until patients experience disease progression or unacceptable side effects.

Patients who added Ibrance had significantly better progression-free survival (PFS), meaning their cancer did not worsen. The median PFS time was 44.3 months in the Ibrance group versus 29.1 months in the control group, Metzger reported. The five-year PFS rates were 43.2% and 33.4%, respectively. The overall response rate, indicating tumor shrinkage, was 29.9% in the Ibrance group compared with 22.2% in the control group.

Overall survival (OS) data are still immature but so far appear to favor Ibrance. The median OS time was 77.0 months in the control group but was not yet reached in the Ibrance group because most patients were still alive. The five-year overall survival rates were 74.3% in the Ibrance group versus 69.8% in the control group.

These results “reinforce the strong scientific rationale for overcoming resistance to anti-HER2 therapy and endocrine therapy with the addition of palbociclib,” according to Metzger.

Treatment was generally safe, but side effects were common; 7.5% of Ibrance recipients stopped treatment for this reason. The most common severe (Grade 3) adverse event in the Ibrance arm was neutropenia, or neutrophil deficiency, which can lead to infections. Moderate to severe fatigue and diarrhea occurred more often in the Ibrance arm. The incidence of life-threatening adverse events (Grade 4 or higher) was similar in both groups (12.3% versus 8.9%). No treatment-related deaths were reported in either group.

Patients who added Ibrance to standard maintenance therapy experienced a “clinically meaningful” 15.2-month PFS improvement with “a manageable toxicity profile,” the researchers concluded. They suggested that Ibrance added to anti-HER2 and endocrine maintenance therapy “may represent a new standard of care” for people with HR-positive/HER2-positive advanced breast cancer.

CDK4/6 inhibitors like Ibrance “should be considered as part of the armamentarium for our patients,” SABCS discussant Sara Hurvitz, MD, of the University of Washington and the Fred Hutchinson Cancer Center, concurred. She called the PFS results in the Ibrance arm “incredible,” but cautioned that nuanced patient selection and more biomarkers to predict response were needed.

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