FDA Approves Keytruda Plus Chemo for Triple-Negative Breast Cancer

First-line treatment with immunotherapy and a chemotherapy regimen extended progression-free survival by 35%.

November 26, 2020 By Liz Highleyman

The Food and Drug Administration (FDA) has granted accelerated approval of the checkpoint inhibitor Keytruda (pembrolizumab) in combination with chemotherapy for the treatment of people with locally recurrent or metastatic triple-negative breast cancer (TNBC) whose tumors express a biomarker associated with better response.

Breast cancer is classified according to the types of receptors it expresses. A majority of breast tumors carry estrogen or progesterone receptors and can be treated with hormone therapy. Others express a receptor called HER2 and can be treated with HER2 inhibitors such as Herceptin (trastuzumab). Triple-negative breast cancer does not express any of these receptors and is harder to treat.

“Approximately 15% to 20% of patients with breast cancer are diagnosed with triple-negative breast cancer, which is a difficult-to-treat and aggressive cancer,” Hope Rugo, MD, of the University of California at San Francisco Helen Diller Family Comprehensive Cancer Center, said in a Merck press release. “The approval of Keytruda in combination with chemotherapy gives physicians an important new option for appropriate patients.”

This approval was based on findings from the Phase III Keynote-355 trial (ClinicalTrials.gov NCT02819518), which included 847 women with previously untreated inoperable locally recurrent or metastatic TNBC. They were randomly assigned to received either Keytruda administered by IV infusion every three weeks or a placebo, in combination with one of three chemotherapy regimens: paclitaxel, Abraxane (protein-bound paclitaxel), or gemcitabine plus carboplatin.

Keytruda, approved for more than a dozen types of cancer, is a monoclonal antibody that blocks PD-1, an immune checkpoint protein on T cells that regulates immune function. Some tumors can hijack PD-1 to turn off immune responses against them. Drugs that block the interaction between PD-1 and its binding partner, known as PD-L1, can release the brakes and restore T-cell activity.

Breast cancer is generally considered a “cold” tumor that doesn’t respond very well to immunotherapy. But combining checkpoint inhibitors with chemotherapy may help make tumors more susceptible.

Tumors with higher PD-L1 levels tend to respond better to this type of checkpoint blocker. Participants in this study were stratified based on whether their tumors were PD-L1 negative, PD-L1 positive (at least 1% expression) or had at least 10% PD-L1 expression. The treatment worked best for those in the latter group, and the recent approval is therefore limited to those with at least 10% PD-L1 expression.

As reported at this year’s American Society of Clinical Oncology Annual Meeting, among the 38% of participants with at least 10% tumor PD-L1 expression, the median progression-free survival (PFS) time was 9.7 months in the Keytruda plus chemotherapy group compared with 5.6 months in the placebo group, reflecting a 35% improvement. Among those with at least 1% PD-L1 expression, the PFS duration was 7.6 months, or a 26% improvement. In the study population as a whole, including those with PD-L1 negative tumors, the PFS time was 7.5 months, an 18% improvement that was not statistically significant. Just over half of participants experienced tumor shrinkage, including 17% with complete remission, according to the Merck press release.

The most common adverse reactions in people treated with Keytruda plus chemotherapy are fatigue, nausea, vomiting, diarrhea, constipation, decreased appetite, hair loss, rash, cough and headache. The combination can cause laboratory abnormalities including low red blood cell, white blood cell and platelet counts and elevated liver enzymes. A quarter of Keytruda recipients in Keynote-355 experienced immune-mediated adverse events related to stepped-up immune activation. Nearly a third of participants experienced serious adverse reactions, and 11% discontinued treatment due to adverse events.

Keytruda is not the first checkpoint inhibitor approved for breast cancer. In 2019, Tecentriq (atezolizumab) plus Abraxane was granted accelerated approval for first-line treatment of people with locally advanced or metastatic TNBC with at least 1% PD-L1 expression. However, the FDA recently issued an alert stating that Tecentriq plus the non-protein-bound form of paclitaxel did not reduce the risk of disease progression or death, and that paclitaxel therefore should not be substituted for Abraxane.

Drugs that receive accelerated approval based on response rates or progression-free survival are expected to undergo further testing to confirm whether they provide clinical benefits such as improved overall survival; the FDA can rescind the approval if they fail to measure up.

Click here for full prescribing information for Keytruda.

Click here to learn more about breast cancer.

Click here to learn more about immunotherapy.

© 2026 Smart + Strong All Rights Reserved.