# Tukysa Regimen Delays Progression of Metastatic Breast Cancer

Adding Tukysa to Kadcyla led to an improvement in progression-free survival, including for patients whose cancer had spread to the brain.

December 7, 2023 By Liz Highleyman

---

Combining Tukysa (tucatinib) and Kadcyla (ado-trastuzumab emtansine) extended progression-free survival for patients with inoperable advanced or metastatic HER2-positive breast cancer, including those with brain metastasis, according to study findings presented this week at the San Antonio Breast Cancer Symposium (SABCS 2023).

Tukysa is an oral tyrosine kinase inhibitor approved in 2020. Kadcyla is an antibody-drug conjugate that uses the HER-targeted antibody trastuzumab (sold alone as Herceptin) to delivers potent chemotherapy directly to tumors. Both medications block HER2, a receptor for a protein that promotes cell growth. Around 20% of breast tumors have high HER2 expression and are susceptible to such treatment. Tukysa, a small molecule, has the added advantage of fighting cancer in the brain, unlike most other HER2-targeted drugs.

“HER2-positive breast cancer has a predilection to spread to the brain, and when this occurs, prognosis is poor. Few options exist for the successful management of breast cancer brain metastases, making this an area of unmet need,” Sara Hurvitz, MD, of the University of Washington and Fred Hutchinson Cancer Center, said in an American Association for Cancer Research news release. “This study is one of very few large breast cancer studies prospectively designed to evaluate novel systemic therapies in patients with brain metastases.”

Previously, the Phase III HER2CLIMB trial (NCT02614794) showed that adding Tukysa to a regimen of trastuzumab plus capecitabine (Xeloda) chemotherapy improved progression-free and overall survival for patients with advanced breast cancer, including those whose cancer had spread to the brain.

To test newer therapies, the Phase III HER2CLIMB-02 trial (NCT03975647) enrolled 463 patients with unresectable locally advanced or metastatic HER2-positive breast cancer, 44% of whom had brain metastasis at baseline. Almost all were women, and the median age was about 54 years. They were randomly assigned to receive twice-daily Tukysa tablets or a placebo along with IV infusions of Kadcyla every three weeks.

The median progression-free survival time was 9.5 months for patients who received Tukysa versus 7.4 months in the placebo group, reflecting a 24% reduction in the risk of disease progression or death, Hurvitz reported. Among patients with brain metastasis, the median progression-free survival times were 7.8 months and 5.7 months, respectively, for a 36% reduction in disease progression or death. Objective response rates, indicating tumor shrinkage, were similar in both groups (42% versus 36%).

With a median follow-up period of about two years, overall survival data are not yet mature. Based on interim data, the median overall survival time was 53 months in the placebo arm but not yet reached in the Tukysa arm.

Treatment was generally safe, though side effects were common overall, and more so in the Tukysa arm. The most frequently reported severe (Grade 3 or higher) adverse events were liver enzyme elevations, anemia, low platelets and fatigue. More people taking Tukysa needed to adjust their doses or  discontinued treatment, but Hurvitz said side effects were largely manageable with monitoring and clinical intervention.

Current practice guidelines do not call for patients with advanced breast cancer to be monitored for brain metastasis unless they experience symptoms. Speaking at a SABCS press briefing, Kate Lathrop, MD, of the Mays Cancer Center at UT Health noted that people with asymptomatic brain metastasis who could potentially benefit from Tukysa are unlikely to be identified. Hurvitz said her findings support reevaluation of brain imaging guidelines, as drugs like Tukysa might delay the need for brain radiation.

Click here for more news about metastatic breast cancer.
Click her for more reports from SABCS 2023.

---