Adding Tukysa to First-line Maintenance Therapy Delays Metastatic Breast Cancer Progression

Benefit was seen across all patients subgroups, including those with brain metastasis.

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Adding Tucatinib to First-line Maintenance Therapy Delayed Disease Progression in HER2-positive Metastatic Breast Cancer in HER2CLIMB-05 Trial

SAN ANTONIO – Adding tucatinib (Tukysa) to first-line maintenance therapy with trastuzumab (Herceptin) and pertuzumab (Perjeta) delayed disease progression in patients with HER2-positive metastatic breast cancer, potentially extending time off chemotherapy, according to results from the Phase III clinical trial HER2CLIMB-05 presented at the San Antonio Breast Cancer Symposium (SABCS), held December 9-12, 2025.

The results of this study were simultaneously published in the Journal of Clinical Oncology.

HER2-positive breast cancer accounts for approximately 17% of all breast cancer cases and is associated with a five-year survival rate of less than 50% for patients with metastatic disease. Since 2012, the first-line treatment for HER2-positive metastatic breast cancer has remained largely unchanged, consisting of chemotherapy followed by maintenance therapy with dual anti-HER2 monoclonal antibodies, said Erika Hamilton, MD, director of Breast Cancer Research at Sarah Cannon Research Institute (SCRI) in Nashville.

Currently, most patients experience disease progression within two years of starting treatment and often have to transition to chemotherapy.

“The results of our study show that the addition of tucatinib to the standard of care represents an enhanced first-line maintenance therapy option for patients with HER2-positive metastatic breast cancer, providing an opportunity to prolong time to disease progression and time off chemotherapy,” said Hamilton, who presented this study.

Tucatinib, a selective inhibitor of HER2, has previously shown efficacy in later lines of therapy, including in patients with brain metastases, according to the results from the HER2CLIMB study, Hamilton said. Based on this, the U.S. Food and Drug Administration approved this drug in 2020

for treatment of unresectable locally advanced or metastatic HER2-positive breast cancer, including patients with brain metastases, following at least one prior therapy.

“The HER2CLIMB-05 trial was initiated to investigate the efficacy of tucatinib in a first-line maintenance setting in patients with HER2-positive metastatic breast cancer who completed chemotherapy-based induction therapy without disease progression,” she said. “We also wanted to assess whether targeting HER2 both intracellularly, with tucatinib, and extracellularly, with dual blockade with monoclonal antibodies, may potentially improve patient outcomes,” she added.

The trial enrolled 654 patients with HER2-positive advanced breast cancer who had completed four to eight cycles of induction chemotherapy plus trastuzumab and pertuzumab, without disease progression. The patients were randomly assigned to receive either tucatinib or a placebo alongside continued trastuzumab and pertuzumab.

At a median follow-up of 23 months, the patients who received tucatinib had a progression-free survival (PFS) of over two years—an improvement of 8.6 months compared with the patients in the control arm.

Patients with hormone receptor (HR)-negative disease experienced a 44.6% reduction in risk of progression or death, with a 12.3-month improvement in median PFS. Those with HR-positive disease saw a 27.5% reduction in risk of progression or death and a 6.9-month improvement in median PFS.

Among the 12.2% of patients with brain metastases at baseline, tucatinib nearly doubled the median central nervous system-PFS, which is the time taken for the cancer to progress to the brain or death from any cause—from 4.3 months to 8.5 months.

“Central nervous system-PFS was a secondary endpoint and this finding is preliminary,” cautioned Hamilton, adding that 54% of the patients in the tucatinib arm remained on study treatment at the data cutoff of this analysis.

These findings suggest that tucatinib may offer broad benefits across diverse patient subgroups, Hamilton said. She emphasized the importance of enhancing HER2 targeting during the maintenance phase, rather than waiting for disease progression. “Prolonging the maintenance phase allows patients to maintain disease control, while extending their time off chemotherapy,” she said.

She noted that the results of the HER2CLIMB-05 trial, alongside recent data from the PATINA trial—where incorporating palbociclib (Ibrance) into the treatment regimen for HR-positive, HER2-positive metastatic breast cancer showed a 15-month improvement in PFS—support a shift toward more personalized first-line maintenance strategies for this patient population.

A limitation of this study is the exclusive enrollment of patients who had not progressed after induction therapy, potentially introducing selection bias, Hamilton explained. Another limitation is that the differences in brain imaging frequency and the cessation of routine imaging after

systemic progression may have affected the accuracy of central nervous system-PFS assessments.

The study was funded by Seagen, which was acquired by Pfizer in December 2023.

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