

WEB EXCLUSIVES

New Agents Effectively Target HER2-Positive Cancers

BY MELISSA WEBER

Herceptin (trastuzumab) and Tykerb (lapatinib), two drugs approved for HER2-positive breast cancer, have greatly improved outcomes for patients, but researchers are now looking for new options to target HER2—a needed approach given that some cancers don't respond while others develop resistance to the drugs.

Two phase II studies presented at SABCS on Friday looked at new agents for patients whose tumors progressed on existing HER2-targeted therapy. The first study looked at trastuzumab-DM1, an intravenous antibody-drug conjugate in which the cell-killing agent DM1 is attached to the Herceptin antibody. After a median follow-up of 19 weeks, 42 of 107 patients with HER2-positive metastatic breast cancer had their tumors shrink by at least half (includes complete responses and partial responses). Final efficacy results will be available next year after all patients have had at least six months of follow-up. Common side effects included thrombocytopenia, fatigue, and infection. No cases of severe cardiotoxicity, a side effect associated with Herceptin, were reported.

Research is under way testing trastuzumab-DM1 as first-line treatment in metastatic HER2-positive breast cancer, but for now, investigators said these data demonstrate trastuzumab-DM1 has anti-tumor activity in Herceptin- and Tykerb-pretreated patients.

The second study tested an oral tyrosine kinase inhibitor called neratinib in metastatic and locally advanced HER2-positive breast cancer. Patients were assigned to one of two arms based on whether they had received prior Herceptin therapy. All patients received a daily oral dose of neratinib. Median progression-free survival—the amount of time the cancer did not progress—reached 23 weeks for the prior Herceptin arm and 40 weeks for the arm that had not received prior Herceptin. Of the 61 patients evaluated in the prior Herceptin arm, 26 percent had their tumors shrink by at least half. For the 66 patients evaluated in the no prior Herceptin arm, 56 percent had tumor shrinkage of at least half.

Diarrhea was the most common side effect, necessitating dose reductions for some patients. Other common side effects included nausea and fatigue. Study investigators concluded that for patients with HER2-positive advanced breast cancer, the clinical activity of neratinib is as good as, if not better than, other HER2-targeted agents.

Future studies will look at the effectiveness of neratinib in combination with Xeloda (capecitabine) as well as how it measures up as a single agent against Tykerb plus Xeloda in a randomized trial.

Read more of *CURE's* coverage of the 31st annual San Antonio Breast Cancer Symposium at <http://media.curetoday.com/html/email/sabcs>.