

Kadcyla Reduces Breast Cancer Recurrence After Surgery

Experts say Kadcyla should become a new standard of care for adjuvant therapy.

December 13, 2018 By [Liz Highleyman](#)

Kadcyla, a medication that combines a targeted antibody with a chemotherapy drug, reduced the risk of breast cancer recurring and spreading after surgery, according to study results presented last week at the San Antonio Breast Cancer Symposium.

Women with HER2-positive breast cancer randomly assigned to use Kadcyla (ado-trastuzumab emtansine or T-DM1) had a 50 percent lower risk of invasive disease recurrence or death compared with those who used Herceptin (trastuzumab), the current standard of care, researchers reported.

Breast cancer is classified by the type of receptors it expresses. A majority of breast cancers are hormone receptor-positive (HR-positive), meaning they carry receptors for estrogen or progesterone; treatment usually includes hormone therapy. Around 20 percent of tumors overexpress HER2 (human epidermal growth factor receptor 2) and can be treated with HER2 inhibitors like Herceptin.

Treatment for HER2-positive early breast cancer typically starts with Herceptin plus chemotherapy to shrink tumors, known as neoadjuvant (presurgery) therapy. This is followed by surgery to remove any remaining cancer. But some cancer cells may be left behind and trigger recurrence. People with residual invasive disease in their surgical specimens—meaning the neoadjuvant therapy was not fully effective—are at greater risk for recurrence and usually receive adjuvant (postsurgery) Herceptin for another year.

Charles Geyer, MD, of Massey Cancer Center at Virginia Commonwealth University, presented findings from the Phase III KATHERINE trial, which compared Kadcyla versus Herceptin for adjuvant treatment in people with residual invasive cancer. The results were also [published in The New England Journal of Medicine](#).

Kadcyla is an antibody-drug conjugate that combines trastuzumab, an antibody directed against HER2 (the same antibody as Herceptin) with emtansine, a cytotoxic drug that interferes with cell division. This enables the antibody to carry the drug into targeted cancer cells. Kadcyla is currently approved for previously treated metastatic breast cancer.

This international trial included 1,486 participants found to have residual invasive cancer in the breast or underarm lymph nodes at the time of surgery, after having undergone neoadjuvant treatment. However, they did not yet have metastatic cancer that had spread to distant parts of the body such as the brain. All had HER2-positive tumors and about three quarters also had HR-positive cancer.

Everyone had used neoadjuvant Herceptin for at least nine weeks, with nearly 20 percent also using the newer HER2 inhibitor Perjeta (pertuzumab). All had used neoadjuvant taxane chemotherapy (drugs like paclitaxel) for at least six cycles, and most had also used anthracyclines (drugs like doxorubicin).

Within three months after surgery they were randomly assigned to receive adjuvant Kadclya or Herceptin given by IV infusion every three weeks for 14 cycles.

An interim analysis showed that 12.2 percent of participants in the Kadclya group developed recurrent invasive cancer or died, compared with 22.2 percent in the Herceptin group. In addition, 10.5 percent of people who used Kadclya had their first recurrence at a distant site compared with 15.9 percent of those who used Herceptin.

At three years post-surgery, 88.3 percent of people in the Kadclya group and 77.0 percent in the Herceptin group were still alive and free of invasive disease—a 50 percent improvement with Kadclya. Differences in overall survival cannot yet be determined and follow-up is ongoing.

Benefits were seen across patient subgroups including both pre- and postmenopausal women, those with HR-positive and HR-negative tumors, those with more or less residual disease at the time of surgery, those with and without cancer in their lymph nodes, and those who did or did not use Perjeta before surgery.

Treatment was generally safe and tolerable. As expected, people who used Kadclya had more side effects than those who used Herceptin. Rates of severe (grade 3 or higher) adverse events were 25.7 percent and 15.4 percent in the two groups; 18.0 percent and 2.1 percent, respectively, stopped treatment for this reason. The most common side effects included fatigue, nausea, headache, joint pain, peripheral neuropathy, low platelet count and elevated liver enzymes, which were mild or moderate.

“I believe these results will be practice-changing,” Geyer said in a conference press release. “The results should form the foundation of a new standard of care in patients with residual invasive breast cancer following neoadjuvant therapy.”

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