

Certain breast cancer patients may benefit from combined HER2 targeted therapy without chemotherapy

April 8 2013

Is the era of targeted therapy for breast cancer at hand? It could be, said experts at the Lester and Sue Smith Breast Center at Baylor College of Medicine – at least for a certain population of women.

In a report that appears online today in the *Journal of Clinical Oncology*, the researchers have shown that a subset of [breast cancer patients](#) who have tumors overexpressing a protein called the human [epidermal growth factor receptor 2](#) (HER-2 positive) may benefit from a combination of targeted treatments that zero in on the [breast cancer cells](#) themselves. That could enable some women to avoid the "sledgehammer" of typical [chemotherapy drugs](#) that kill normal and [tumor cells](#) alike and avoid triggering resistance in tumor cells.

"This study really epitomizes the whole new era of cancer medicine, using effective targeted treatments against selected subsets of [patients](#) resulting in high efficacy," said Dr. Mothaffar Rimawi, medical director of the Smith Breast Center and first author on the study. "If we can efficiently target factors important to an individual's tumor, we can shut down the cancer. If we are not efficient, we are training the tumors to be resistant and develop other tumor drivers."

"By using two drugs that target the HER-2 pathway, we can attack the tumor in multiple ways and shut down its growth," said Rimawi.

The clinical trial (TBCRC 006) involved 64 women with large tumors that tested positive for HER-2 and some that were also estrogen-receptor positive. Using two drugs – lapatinib (brand name Tykerb®) and trastuzumab (brand name [Herceptin](#)) – that target HER-2 in different ways, physicians were able to eliminate all [clinical evidence](#) of the disease in 36 percent of estrogen-receptor negative patients and 21 percent of estrogen receptor-positive patients, the researchers reported.

Patients whose tumors tested positive for the estrogen receptor which meant that their tumor grew in response to the [female hormone](#) received another drug called an aromatase inhibitor to stop production of estrogen.

Preclinical models developed at BCM

"We have shown in the laboratory that complete blockage of the HER-2 family including HER-1, 2 and 3 with the drugs lapatinib and trastuzumab leads to eradication of HER-2 positive tumors in mice," said Rimawi. "These drugs alone only partially inhibit the pathway, quickly resulting in resistance to treatment."

Rimawi developed this model in 2004 as a fellow in the laboratory of Dr. C. Kent Osborne, director of both the Smith Breast Center and the NCI-designated Dan L. Duncan Cancer Center at BCM and the co-senior author on the report, and Dr. Rachel Schiff, associate professor in the Smith Breast Center, also a co-author on the paper.

Over the last 10 years, researchers have tested both targeted drugs – lapatinib and trastuzumab – in studies in the patients. In the laboratory, Rimawi and colleagues demonstrated that the two drugs would likely work better when used together.

The research team at BCM sought to translate these findings to patients,

so they initiated a multicenter clinical trial through the Translational [Breast Cancer](#) Research Consortium.

Rimawi and his team observed that tumors disappeared in many patients in this clinical trial, just as they had in the laboratory animals, said Osborne.

Study design

The trial involved patients from the Smith [Breast Center](#) (at the Baylor Clinic and the Harris Health System's Ben Taub Hospital sites), the Vanderbilt University School of Medicine, the University of Alabama at Birmingham, the University of Chicago and the Mayo Clinic College of Medicine.

The patients had large HER-2 positive tumors in the breast when they were initially diagnosed. They received a combination of lapatinib daily and trastuzumab (Herceptin®) once weekly for 12 weeks before surgery.

They did not receive standard anti-cancer drugs. Lapatinib is a pill that blocks the enzyme activity of HER-2 and its close family member HER-1. Trastuzumab is an antibody administered intravenously that blocks HER-2 in a different way.

"With this combination, we are able to block all of the cancer-promoting signals from the HER family, which we know is crucial for growth of this kind of breast cancer," said Osborne. "Each of these drugs hits a different receptor, thereby shutting down the pathway responsible for the breast cancer's growth."

Study results

After 12 weeks, 36 percent of the estrogen-receptor negative, HER-2 positive patients had eradication of invasive breast cancer, which is "the type of breast cancer that can spread beyond your breast and invade healthy, surrounding tissue, and other organs," said Rimawi.

A significant benefit was also observed in the estrogen-receptor positive group, Rimawi said.

"Twenty-one percent of these patients had complete disappearance of their tumors and another 33 percent had near eradication with only small amounts of tumor left after treatment."

"We have seen similar results in other recently reported studies using the lapatinib/trastuzumab combination, but this is the first study not to use chemotherapy," said Osborne. "The side effects of chemotherapy can be significant and eliminating the need for chemotherapy in certain patients would represent a groundbreaking approach to treatment."

The women in the study were ethnically and racially diverse, with 33 percent Hispanic and 21 percent African-American.

Next steps in research

"Our next step with this research will be to determine the optimal duration of treatment," said Rimawi. Studies are underway now to identify which patients can be safely treated without chemotherapy for this subtype of breast cancer.

More information: This study was supported by GlaxoSmithKline and the Translational Breast Cancer Research Consortium.

Provided by Baylor College of Medicine

Citation: Certain breast cancer patients may benefit from combined HER2 targeted therapy without chemotherapy (2013, April 8) retrieved 23 April 2024 from <https://medicalxpress.com/news/2013-04-breast-cancer-patients-benefit-combined.html>

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