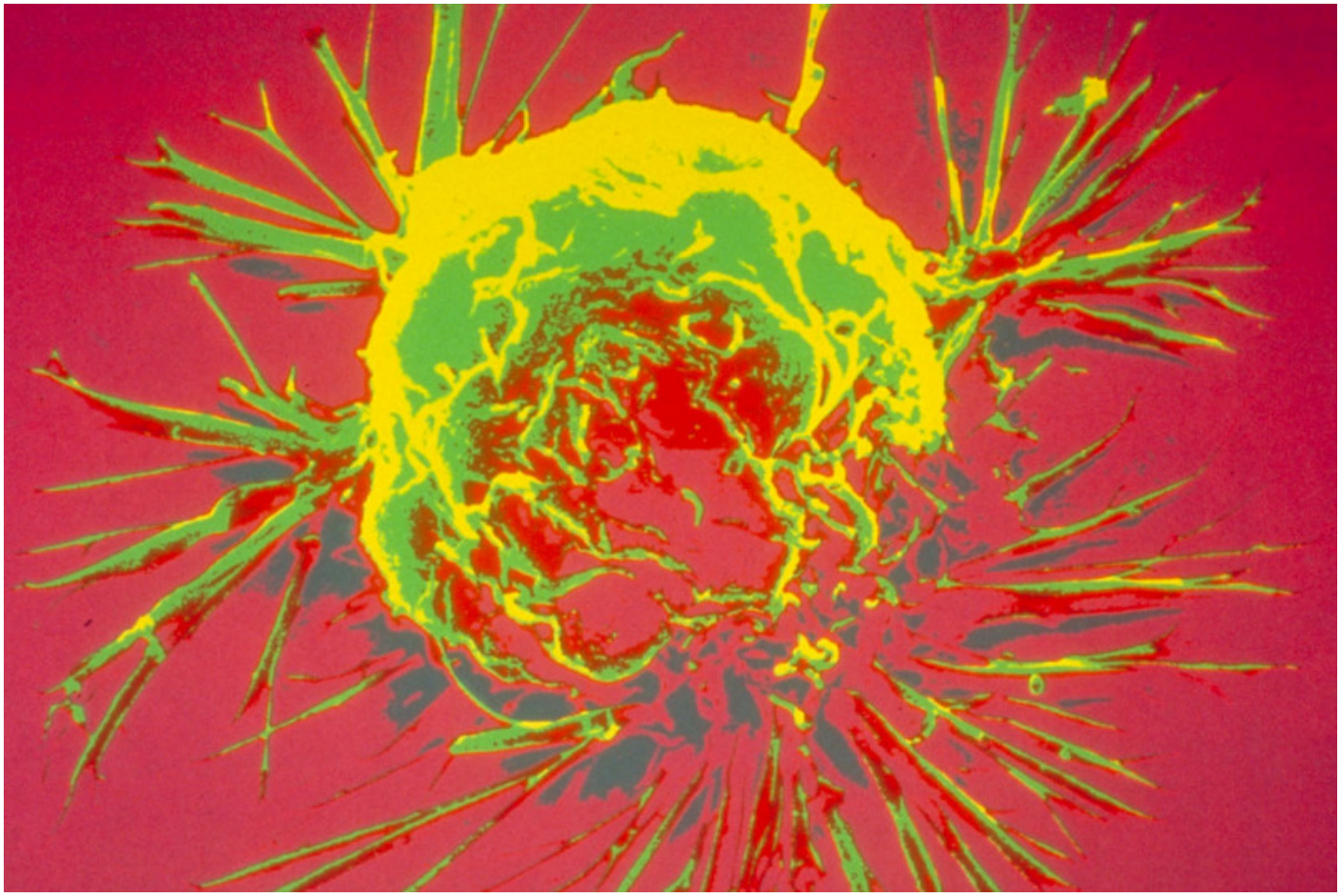
On Cancer

Targeted Drug Shows Promise Against HER2-Positive Breast Cancer That Stops Responding to Other Drugs

By Julie Grisham, **Wednesday, December 11, 2019**



A protein called HER2 drives the growth of many breast cancer cells. Image credit: National Cancer Institute/Science Source

Summary

A new study in the *New England Journal of Medicine* details the results from a phase II trial of a breast cancer drug called trastuzumab deruxtecan or DS-8201a. MSK medical oncologist Shanu Modi is the lead author of the paper, which was also presented at the San Antonio Breast Cancer Symposium.

Update: On December 20, 2019, the FDA approved trastuzumab deruxtecan (Enhertu®) for people with unresectable (unable to be removed with surgery) or metastatic HER2-positive breast cancer who have previously received at least two anti-HER2-based treatments for metastatic disease.

About 15 to 20% of **breast cancer** that has spread (metastatic cancer) is driven by a protein called HER2. Drugs that target HER2 are a critical tool for bringing this form of the disease under control. Unfortunately, most cancers eventually stop responding to HER2 drugs and begin growing again. Because of this, many breast cancer experts are focused on developing new ways to target HER2.

At this year's San Antonio Breast Cancer Symposium, which is being held December 10 to 14, Memorial Sloan Kettering medical oncologist **Shanu Modi** was part of a multicenter group that presented findings from a phase II clinical trial of an experimental drug targeted at HER2-positive metastatic breast cancer. Dr. Modi is also the lead author of a paper detailing the results from the trial, which was **published December 11 in the *New England Journal of Medicine***. The drug is called trastuzumab deruxtecan or DS-8201a.

"There are already two great options for treating HER2-positive metastatic breast cancer, and these existing drugs can provide people with months or years of controlled disease," Dr. Modi explains. "But once they stop working, there is no standard approach. Therefore, there is a lot of excitement around new HER2-targeting drugs."

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DS-8201a is a type of medication called an antibody-drug conjugate. It consists of two parts: an antibody called trastuzumab attached to chemotherapy. The trastuzumab antibody is designed to seek out the HER2 protein. When it finds it, it delivers its payload of chemotherapy directly to the tumor, sparing healthy tissue.

DS-8201a is not the first antibody drug-conjugate developed for breast cancer. A drug called **ado-trastuzumab emtansine (Kadcyla®)** works in the same way but carries a different chemotherapy drug. That drug was approved by the US Food and Drug Administration for metastatic breast cancer in 2013. Antibody drug-conjugates are used to treat other types of cancer as well, especially blood cancers.

“DS-8201a appears to work in people who have stopped responding to ado-trastuzumab emtansine,” Dr. Modi says. “One reason why is that DS-8201a has twice as many molecules of chemotherapy linked to each antibody. Additionally, the chemotherapy that’s attached has some unique properties that make it very effective.”

Another Approach for a Challenging Disease

In the phase II study, called the DESTINY01 trial, 184 patients received DS-8201a by IV every three weeks. The participants had previously received trastuzumab and ado-trastuzumab emtansine but had stopped responding to them. More than 60% of the patients responded to DS-8201a. That means their tumors either shrank or stopped growing.

The average time from when patients received the drug until the tumors started growing again was about 16 months. Although there was no direct comparison to other therapies in this trial, these results are much better than the responses seen with other treatments given at this stage of treatment, usually chemotherapy, Dr. Modi explains.

The common side effects from the drug were nausea and lowered blood counts, and these were easily managed with medication. However, a small number of people in the trial had a severe response: They developed a condition called interstitial lung disease, which means their lungs developed scarring, leading to difficulty breathing. This risk was first noted in the phase I trial.

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Shanu Modi
medical oncologist

In this phase II study, because the doctors knew that this could occur, patients were monitored very carefully. Anyone who developed lung problems or other severe side effects was taken off the drug. However, four people in the phase II trial died from interstitial lung disease.

Based on the findings from this trial, three large, multicenter phase III trials are already underway. Two of them are open at MSK, including **one trial** for people with lower levels of HER2. Dr. Modi expects MSK to be one of the main hospitals to recruit people for the trial.

“This disease is so challenging to treat, and the responses we’ve seen so far are amazing,” she concludes. “I felt good every time I was able to enroll one of my patients in this trial.”

This study was funded by Daiichi Sankyo, the company that developed DS-8201a. Daiichi Sankyo and AstraZeneca were collaborators on the study.

Dr. Modi has consulted for or served on the advisory boards of Genentech, Carrick Therapeutics, MacroGenics, Puma, GlaxoSmithKline, Novartis, AstraZeneca, Seattle Genetics, and Eli Lilly. She has served on the Genentech Speakers Bureau. She has also received compensation from Daiichi Sankyo for advisory services.

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