

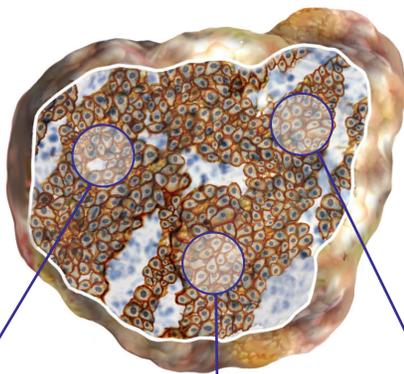
Differences Between HER2 Testing in Breast and Stomach Cancers

Interpretation of HER2 testing is different for breast and stomach cancers. Though similar tests are used, improper testing procedures may impact the determination of HER2 status and subsequent treatment.

DIFFERENCES INCLUDE:

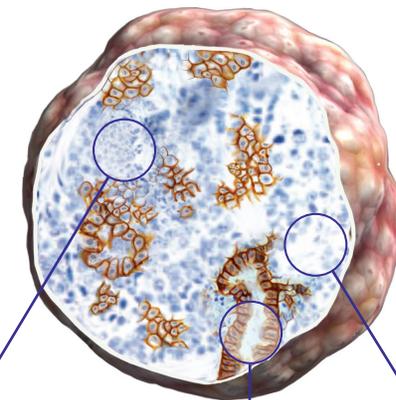
- More tumor tissue samples generally need to be examined for determining HER2 status in stomach cancer.
- Distribution of HER2-positive cells in the tumor tissue tends to be different for breast and stomach cancers.
- The staining pattern of the cell membrane is different for breast and stomach cancer tumor tissues.
- The scoring and interpretation of the test results for breast and stomach cancers are different.

HER2-POSITIVE BREAST CANCER TUMOR



**DISTRIBUTION OF HER2-POSITIVE
CANCER CELLS IS DIFFERENT FOR
BREAST AND STOMACH CANCERS**

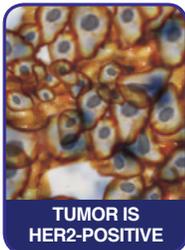
HER2-POSITIVE STOMACH CANCER TUMOR



Tumor Biopsies

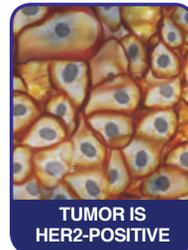
- Very thin slices of the tumor are cut and stained with specific dyes to identify HER2 protein
- Stained slices are examined under a microscope

BIOPSY 1



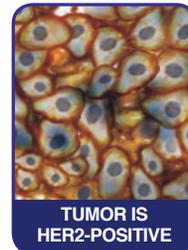
TUMOR IS
HER2-POSITIVE

BIOPSY 2



TUMOR IS
HER2-POSITIVE

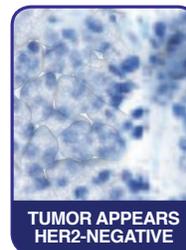
BIOPSY 3



TUMOR IS
HER2-POSITIVE

Staining pattern of cell membrane as well as the number and arrangement of stained tumor cells are different in HER2-positive breast and stomach cancers

BIOPSY 1



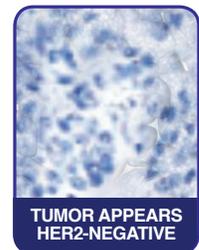
TUMOR APPEARS
HER2-NEGATIVE

BIOPSY 2



TUMOR IS
HER2-POSITIVE

BIOPSY 3



TUMOR APPEARS
HER2-NEGATIVE

Less tumor tissue is generally needed for breast cancer HER2 testing because HER2-positive breast cancer tumor cells are more likely to be evenly distributed. Generally, one biopsy sample may be sufficient to determine HER2 status for breast cancer.

In HER2-positive stomach cancer tumors, not all biopsies look HER2-positive due to uneven distribution of HER2-positive cells. Seven to eight biopsies may be needed for accurate HER2 testing. Not all biopsies have to be HER2-positive for a HER2-positive diagnosis.

About Herceptin

Herceptin is a targeted medicine (not a chemotherapy) designed to specifically block the HER2 protein on the surface of some cancer cells. Based on preclinical studies, Herceptin may work by attaching to HER2 receptors to stop signals that make the tumor cells grow and divide, and also by signaling the body's immune system to destroy the cancer cells.

Adjuvant Breast Cancer:

Herceptin is approved for the treatment of early-stage breast cancer that is **Human Epidermal growth factor Receptor 2-positive (HER2+)** and has spread into the lymph nodes, or is HER2+ and has not spread into the lymph nodes. If it has not spread into the lymph nodes, the cancer needs to be estrogen receptor/progesterone receptor (ER/PR)-negative or have one high risk feature.* Herceptin can be used in several different ways:

- As part of a treatment course including the chemotherapy drugs doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel. This treatment course is known as "**AC → TH**"
- With the chemotherapy drugs docetaxel and carboplatin. This treatment course is known as "**TCH**"
- Alone after treatment with multiple other therapies, including an anthracycline-based therapy (a type of chemotherapy)

*High risk is defined as ER/PR-positive with one of the following features: tumor size >2 cm, age <35 years, or tumor grade 2 or 3.

Metastatic Breast Cancer:

Herceptin has two approved uses in metastatic breast cancer:

- Herceptin in combination with the chemotherapy drug paclitaxel is approved for the first line treatment of **Human Epidermal growth factor Receptor 2-positive (HER2+)** metastatic breast cancer
- Herceptin alone is approved for the treatment of HER2+ breast cancer in patients who have received one or more chemotherapy courses for metastatic disease

Metastatic Gastric Cancer:

Herceptin is approved in combination with the chemotherapy drugs cisplatin, and either capecitabine or 5-fluorouracil, for metastatic HER2-positive stomach cancer or cancer of the gastroesophageal junction, in men and women who have not received prior medicines for their metastatic disease.

IMPORTANT SAFETY INFORMATION

- **Herceptin treatment can result in heart problems, including those without symptoms (such as reduced heart function) and those with symptoms (such as congestive heart failure). One patient died in an adjuvant (early) breast cancer trial from significantly weakened heart muscle. The risk and seriousness of these heart problems were highest in people who received both Herceptin and a certain type of chemotherapy (anthracycline).**
- Before taking the first dose of Herceptin and during treatment, a patient's doctor should check to see if there are any health conditions that may increase the patient's chance of having serious heart problems. This includes a review of the patient's health history and tests to see how well the heart muscle is working. These tests may include an echocardiogram or a MUGA scan. Some early breast cancer patients may also need to have a test done after they have finished taking Herceptin to see how well their heart muscle is working.
- **Some patients have had serious infusion reactions and lung problems; fatal infusion reactions have been reported. These reactions usually occur during or within 24 hours of receiving Herceptin.**
- **The patient's doctor may need to completely stop Herceptin treatment if the patient has a severe allergic reaction, swelling, lung problems, inflammation of the lung, or severe shortness of breath.**
- **Herceptin can cause harm to the fetus (unborn baby), in some cases death to the fetus, when taken by a pregnant woman.** Women who could become pregnant need to use effective birth control methods during Herceptin treatment and for at least 6 months after treatment with Herceptin. Nursing mothers treated with Herceptin should discontinue nursing or discontinue Herceptin.
- Worsening of low white blood cell counts associated with chemotherapy has also occurred.
- Patients must have a HER2 test to determine if their breast or stomach cancer is HER2-positive before using Herceptin, as benefit has only been shown in patients that are HER2-positive.
- The most common side effects associated with Herceptin in patients with breast cancer are fever, nausea, vomiting, infusion reactions, diarrhea, infections, increased cough, headache, fatigue, shortness of breath, rash, low white and red blood cells, and muscle pain.
- The most common side effects associated with Herceptin in patients with stomach cancer are low white blood cell counts, diarrhea, fatigue, low red blood cell counts, inflammation of the lining of the mouth, weight loss, upper respiratory tract infections, fever, low platelet counts, swelling of mucus membranes, swelling of the nose and throat, and a change in taste.
- Because everyone is different, it is not possible to predict what side effects any one person will have. Patients with questions or concerns about side effects should talk to their doctor.
- Patients should read the Herceptin Full Prescribing Information including Boxed WARNINGS, at www.herceptin.com.