Genentech
BIOONCOLOGY™

FACT SHEET

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HER2 Testing Fact Sheet

Testing tumors to determine their genetic makeup provides vital information about cancer at the cellular level. Together with physical characteristics, such as size, type and stage of the tumor, tumor marker testing can help determine the appropriate medicines needed to treat the disease most effectively. A variety of tests to identify breast and stomach (gastric) cancer tumor markers can be performed.

Herceptin® (trastuzumab) 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.

Who Should Be Tested

- Guidelines from various organizations recommend people with breast cancer receive tumor marker testing, including the American Society of Clinical Oncology (ASCO), the College of American Pathologists (CAP) and the National Comprehensive Cancer Network (NCCN).[1,2,3]
- No guidelines exist yet for stomach cancer testing.
- A person who had a biopsy (a tissue sample taken from the tumor for testing), but has not received a tumor marker test, may request it from his or her doctor.
- If a person is told their sample is no longer being stored, a new biopsy may be requested if the tumor is still present or if the cancer returns.
- People should ask their doctor for additional information about testing.

HER2 Testing For Breast and Stomach Cancer

- Standard human epidermal growth factor receptor 2 (HER2) tests measure if there is a higher than normal number of HER2 genes present in tumor cells or if there is a higher than normal number of HER2 receptors on the surface of tumor cells.
  - HER2 Fluorescence *in-situ* Hybridization (FISH) – a gene-based diagnostic test used to identify people whose breast or stomach cancer cells carry amplified HER2 genes and therefore make too much HER2 protein.[1]
  - HER2 Immunohistochemistry (IHC) – a protein-based diagnostic test used to identify people whose breast or stomach cancer cells overexpress the HER2 protein as a result of too many copies of the HER2 gene.[1]
- A tumor may be HER2-positive if the test shows a higher than normal number of HER2 genes or receptors.

- There are distinct differences between stomach and breast cancers. The HER2 testing process (such as scoring and interpretation of results) is different for stomach and breast cancers. Though similar testing methods are used, improper testing procedures may impact the determination of HER2 status and subsequent treatment. Differences include:
  - A u-shaped staining pattern may be seen when stomach cancer cells are stained for testing compared to the circular staining pattern seen with breast cancer cells.
  - HER2-positive stomach cancer cells may be distributed more unevenly throughout the tumor compared to breast tumors.
  - There may be less tumor tissue available for testing from stomach biopsies compared to breast biopsies.
- Interpretation and scoring of HER2 FISH and IHC tests must take these differences into account to avoid potential mistakes that may lead to inaccurate test results.[1]
- In both breast and stomach cancers, specialized training and experience are needed to help ensure HER2 tests are accurately performed and the results are accurately interpreted.
- Approximately 25 percent of breast cancers are HER2-positive.[4,5]
- In screening patients for HER2 status for the ToGA pivotal trial, 22 percent were found to be HER2-positive.[6]
- Assessment of HER2 status is needed to decide if treatment with Herceptin is appropriate.[1,7]

Genentech is committed to making a difference in the lives of patients with serious and life-threatening diseases. We continue to learn more about which people may benefit most from our medicines. During the clinical development process for all of our marketed and pipeline medicines, Genentech evaluates tumor markers and diagnostics that may help healthcare providers identify appropriate patients for our medicines.

About Herceptin

Adjuvant Breast Cancer:
Herceptin is approved for the treatment of early-stage breast cancer that is **H**uman **E**pidermal growth factor **R**eceptor **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 **c**arboplatin. 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 **H**uman **E**pidermal growth factor **R**eceptor **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 Including Serious Side Effects

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.

References

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