Understanding HER2 Testing and Treatment

Breast Cancer™
NETWORK of STRENGTH

formerly known as Y-ME National Breast Cancer Organization

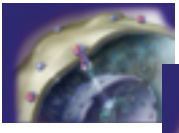
We're here today for those who can't wait for tomorrow's cure.

What is HER2?

According to the American Cancer Society, about 15 percent to 30 percent of people with breast cancer test positive for HER2.[1] HER2-positive breast cancer contains a protein called human epidermal growth factor receptor-2 (HER2). Too much HER2 promotes the growth of cancer cells.[2] As a result, these tumors tend to grow faster and are more likely to recur (come back) than other types of tumors.[3]

How it Works

The HER2 protein is a receptor on the surface of the normal cells that sends messages to the cell to grow and divide more frequently.[4] In HER2-positive cancers, there is too much HER2 protein, which can cause a tumor to grow more aggressively.



Normal

Overexpressed HER2

Excessive cellular division

Kallioniemi et al, *Proc Natl Acad Sci U S A* 1992;
Sliwkowski et al, *Semin Oncol* 1999

What it Means for You

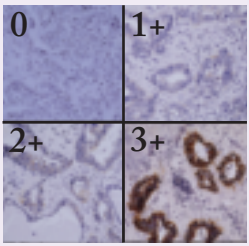
HER2 is a tumor marker that is found in some breast cancer cells. Tumor markers are materials, usually proteins, that can be found in the body when cancer is present. They help doctors evaluate treatment options and prognosis (outcome) for the patient. Unfortunately, patients who test positive for HER2 may not respond well to chemotherapy and generally have a less favorable prognosis than patients with other types of breast cancer.[5]

Getting Tested

Having your tumor tested to find out its HER2 status is important and will help your doctor determine the best treatment for you. There are two tests available: IHC (immunohistochemistry) and FISH (fluorescence in situ hybridization).

IHC (Immunohistochemistry)

IHC assesses the amount of HER2 protein on the surface of cancer cells. It is performed by a pathologist in a laboratory. The test involves analyzing a sample of the tumor that was removed during a biopsy, lumpectomy or mastectomy.[6] The surface of the cell is stained with an antibody. The pathologist judges the degree of color change in the cell to determine the level of HER2.[7] The results of the test are measured on a scale from 0 (negative) to 3+ (strongly positive). Patients with tumors that are 2+ are considered borderline; the National Comprehensive Cancer Network (NCCN) recommends performing a FISH test to determine whether the tumor is HER2-positive.[6]



HER-2 as assessed by IHC

Benefits of the IHC test:

- Quick
- Less expensive than the FISH test

Drawbacks of the IHC test:

- The protein being measured can be damaged during preparation of the tissue sample, ruining the outcome of the test;
- Evaluation of the sample is subjective;
- False positive or false negative test results can occur.

FISH (Fluorescence In Situ Hybridization)

FISH measures the number of copies of the HER2 gene in the cells of the tumor. THE HER2 gene provides the blueprint for the manufacture of the HER2 protein. Tumors with too many copies are considered HER2-positive.[3] The FISH test is done by a pathologist in a laboratory on a sample of a tumor removed during a biopsy, lumpectomy or mastectomy. The test "highlights" the HER2 genes inside the cell, making them appear fluorescent so they may be counted.[7] A FISH score greater than 2 means that there are more than two genes per cell and the tumor is HER2-positive. Sometimes a score can be in the borderline range. When this happens, the National Comprehensive Cancer Network (NCCN) recommends counting additional cells in the tissue sample, retesting with FISH or performing an IHC test.

Reliable Results

The left photo shows HER2 non-amplified (ratio <2)
The right two photos show HER2 amplified (ratio >2)

Benefits of the FISH test:

- Because genes are counted, it is a more objective assessment than IHC;[7]
- More accurate than IHC.

Drawbacks of the FISH test:

- False positive or false negative test results can occur;
- It is more difficult and more expensive than IHC.[8]

Which Test Should I Get?

The most common practice in the United States is to first screen patients using IHC. However, most experts believe that the FISH test is more accurate. That is why tumors that test 2+ must be retested with FISH. **If IHC was used and your test result is 2+, you should request a FISH test.**

Treatment Options

Trastuzumab (brand name: Herceptin®) and lapatinib (brand name: Tykerb®) are the two medications approved by the U.S. Food and Drug Administration to treat HER2-positive breast cancer. However, new treatments are being developed all the time, so you should talk to your doctor about what's right for you.

Trastuzumab (Herceptin)

The drug trastuzumab is an effective HER2 treatment[4] and is given to the patient by injection.[9] It is a manmade antibody that blocks the action of HER2 from outside the cancer cells to slow down their production.[5] It specifically targets and binds to the HER2 receptors on the tumor cell surface. It may also work with chemotherapy to destroy HER2-positive cancer cells.[4]

Patients with tumors that are HER2-positive as indicated by FISH or IHC are most likely to benefit from trastuzumab. Patients with tumors that test negative are unlikely to benefit from this treatment.[3]

Possible side effects of trastuzumab include:

- Fever
- Chills
- Pain
- Weakness
- Nausea
- Vomiting
- Diarrhea
- Headaches
- Difficulty breathing
- Rashes
- Heart muscle damage that can lead to heart failure
- Severe allergic reactions such as a drop in blood pressure, shortness of breath, rashes and wheezing

Patients who receive Herceptin along with chemotherapy may experience side effects such as anemia and upper respiratory infections.[3]

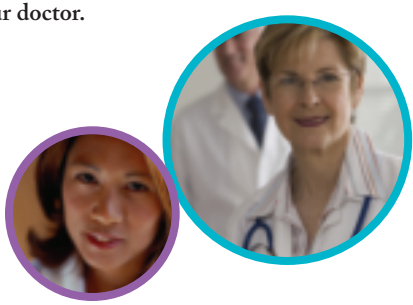
Lapatinib (Tykerb)

Lapatinib is a newer drug that was approved by the FDA in March 2007. It is a targeted treatment to be used in combination with capecitabine (brand name: Xeloda®) for patients with advanced or metastatic breast cancer (has spread to other parts of the body) that is HER2-positive.[10] Lapatinib is known as a "kinase inhibitor," blocking the effects of HER2 from the inside of the cell. It is recommended for patients who did not respond successfully to Herceptin.

Possible side effects of lapatinib include:

- Diarrhea
- Nausea
- Vomiting
- Rash
- Hand-foot syndrome that may include numbness, tingling, redness, swelling and discomfort of hands and feet
- Reversible decreases in heart function that can lead to shortness of breath[10]

It is important to discuss the possible side effects of treatment with your doctor.



1 www.cancer.org/downloads/STT/CAFF2007PWSecured.pdf
2 www.mayoclinic.com/health/breast-cancer/AN00495
3 www.cancer.gov/cancertopics/factsheet/therapy/herceptin
4 www.nccn.org/patients/patient_gls/_english/_breast/5_treatment.asp
5 www.cancer.org/docroot/PED/content/PED_2_3X_Tumor_Markers.asp?sitearea=PED
6 www.nccn.org/patients/patient_gls/_english/_breast/3_work-up.asp
7 www.pathvysion.com/TypesofHER2Testing_914.aspx
8 www.nccn.org/patients/fact_sheet.asp
9 www.susanlovemd.com/breastcancer/content.asp?CATID=20&L2=3&L3=7&L4=0&PID=&sid=132&cid=580
10 www.fda.gov/bbs/topics/NEWS/2007/NEW01586.html

Questions to ask your doctor:

Be sure to speak with your health care team about any concerns you have. You may want to bring this list of questions to your next appointment to help start the conversation.

- What does being HER2-positive or HER2-negative mean for me?
- Why should I be tested?
- Is the test covered by insurance?
- Which test will be used to determine my HER2 status?
- When will I know the results?
- Will I need a follow-up test?
- How will my treatment be determined?
- What are my treatment options?
- What are the possible side effects of my treatment?

What other questions do you have?

Write them below to help you remember.

We're here if you need us

If you would like to speak with other breast cancer survivors about how they coped with HER2 testing and treatment, our specially trained YourShoes peer counselors are available to answer your questions 24 hours a day. You are not alone. We're here to help.

Breast Cancer™
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formerly known as Y-ME National Breast Cancer Organization

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