HER2-NEU POSITIVE BREAST CANCER

What is Her2-neu?

Her2-neu is a receptor that belongs to the Epidermal Growth Factor Receptor group of receptors (simply called EGFR). Her2 is a receptor for a particular growth factor called Human Epidermal Growth Factor, which is a protein molecule occurring naturally in the body and is present in a cancer cell or its microenvironment. When human epidermal growth factor attaches itself to Her2 receptors on breast cancer cells, it can stimulate the cells to divide and grow. These receptors on the surface of a cancer cell act as ignition switches. Approximately 30% of breast cancers are positive for Her2.

Why is Her2-neu important?

When your doctor informs that you are Her2 Positive it means two things. Good news and a bad news! Her2-neu receptor presence on the cancer cell suggests a more aggressive form of breast cancer which is associated with increased disease recurrence and worse prognosis. They grow faster and have an increased potential of spreading to lymph-nodes and other organs.

The good news is that, the presence of this switch gives us an important therapeutic advantage as we can specifically target and destroy cancer cells without jeopardizing other body cells. There are drugs that specifically target the Her2 switch and turn it off. Turning off the switch makes the cancer cells less aggressive and prevents their growth. Trastuzumab (herceptin) and Lapitinib (tykreb) are drugs that are highly effective in blocking this receptor/switch. These drugs are not as harsh as other forms of cancer therapy. Not all breast cancers have an advantage of being dealt with such targeted therapies, and Oncologists are forced to use only chemotherapy which is less specific.

How is Her2-neu tested?

When a breast biopsy is performed, the tissue obtained is sent to a pathologist. There are two methods of testing for Her2 tumor status in women with breast cancer: Immunohistochemistry (IHC) and Fluorescence in Situ Hybridization (FISH). Results from both tests are used in the clinical setting.

IHC: It is a protein-based test that is used to provide an assessment of the amount of Her2 protein receptors on the surface of the cancer cells. In Her2-positive tumors there is more than a normal amount of HER2 protein on the cell surface.

Analysis time is 1 to 3 days.

The IHC test is done by a pathologist in a laboratory on a sample of a tumor removed during a biopsy, a lumpectomy or a mastectomy. The sample of tumor is exposed to an antibody which attaches to the Her2 receptors, reacts with other substances that cause a color change in the tissue sample. Based on the number of cells stained and intensity of color change in the cells of the sample, the score for the test is determined. The scoring for an IHC test is from 0 to 3+.
- Zero is Her2 negative
- 1+ is considered Her2 negative
- 2+ is considered a borderline or equivocal result
- 3+ is Her2 positive

An equivocal result is confirmed with FISH.

**FISH:** It is a gene-based test used to determine the number of Her2 genes in the cells of the tumor. It is considered more accurate to determine Her2 tumor status.
Analysis time 2 to 4 days.
The interpretation of this test involves determination of Ratio of Her-2neu:CEP 17 control.

**Ratio:**
- <1.8 = negative for Her-2neu amplification
- 1.8 to 2.2 = equivocal
- >2.2 = positive for Her-2 neu amplification

An equivocal result is confirmed by repeating FISH or counting additional cells.

**TREATMENT QUERIES**

**How is Trastuzumab (herceptin™, Genentech) given?**

Trastuzumab is effective against tumors that over-express the Her2-neu protein.
Trastuzumab (herceptin) is given as Intravenous infusion. First dose is given over 90 minutes. If well-tolerated, subsequent maintenance doses may be given over 30 minutes. It can be given either weekly or every three weeks as a larger dose.
The amount of trastuzumab that you will receive depends on many factors, including your height and weight, your general health or other health problems.

**Can I take an oral Her2-neu receptor blocker?**

Lapatinib is FDA approved for Her2-neu receptor positive breast cancer and is taken orally, one hour before or after food.

**What type of side effects can I expect from Trastuzumab or Lapatinib?**

Not all side effects are experienced by patients. The side effects are often predictable in terms of their onset and duration, almost always reversible and will go away after treatment is complete. There are many options to help minimize or prevent these side effects.

*Common side effects of transtuzumab:*
- Chills or fever during first infusion
- Body pain (Ibuprofen may help)
- Weakness (Adequate rest and good nutrition may help)
- Nausea (Eat small frequent meals)
A serious but uncommon side effect of trastuzumab can be interference with the pumping action of the heart. The incidence of heart problems increase in people with heart disease or other risk factors such as radiation to the chest, advancing age, and use of other heart-toxic drugs. Doctors usually check your heart function before administration of trastuzumab and also monitor your heart function closely during your treatment. Trastuzumab may be discontinued if symptoms of heart failure appear e.g. fatigue, shortness of breath or exercise intolerance.

**Common side effects of lapatinib:**
- Diarrhea
- Rash on palms and feet
- Liver enzyme problems
- A serious but uncommon side effect: weakening of heart muscle and rhythm problems

**Notify your health care provider, if you experience the following symptoms:**

- Symptoms of heart failure: Shortness of breath, difficulty breathing and fatigue;
- Symptoms of allergic reaction: Facial swelling, hives and wheezing.

---

DR. JIGISHA P THAKKAR, MBBS, VISITING RESEARCH ASSOCIATE, UNIVERSITY OF ILLINOIS AT CHICAGO.

DR. DIVYANG SHARMA, MEDICAL STUDENT, UNIVERSITY COLLEGE OF MEDICAL SCIENCES (GTB HOSPITAL), DELHI