Approximately 25% of people with breast cancer are HER2-positive, an aggressive form of the disease. Genentech has developed personalized medicines specifically for this type of cancer.

**Stages of Breast Cancer and Impact on Treatment**

Early-stage breast cancer (Stages I and II) is different from advanced breast cancer (Stages III and IV). Most people with advanced breast cancer will receive medicine for the rest of their lives.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Tumor is limited to the breast (&lt;2 cm)</td>
</tr>
<tr>
<td>II</td>
<td>Tumor has spread to 1-2 lymph nodes in the breast (&lt;5 cm)</td>
</tr>
<tr>
<td>III</td>
<td>Tumor has spread to 4-9 lymph nodes or to the chest wall or skin</td>
</tr>
<tr>
<td>IV</td>
<td>Tumor has spread to distant organs</td>
</tr>
</tbody>
</table>

A person’s treatment may depend on whether he or she has:

- **EARLY-STAGE Breast Cancer**
  - Previously untreated — has not yet received treatment for advanced disease or the disease has come back after prior therapy for early-stage cancer

- **ADVANCED Breast Cancer - Previously Untreated**
  - Previously treated — has already received initial treatment for advanced disease, but the cancer has gotten worse

**REFERENCES**

HERCEPTIN®
(trastuzumab)1,2

HERCEPTIN® is approved for early-stage breast cancer in a HER2-positive patient and has also been used to treat advanced disease. When HER2 is overexpressed, the cancer must be trastuzumab-positive (ERBB2)/negative or have high HER2 levels.3 HERCEPTIN® can be used in several different ways:

- With the chemotherapies doxorubicin, cyclophosphamide, and paclitaxel or docetaxel.
- With the chemotherapies docetaxel and carboplatin.

*High risk is defined as ERBB2-positive with one of the following features: tumor size >2 cm, age <35 years, or tumor Grade 2 or 3.
Herceptin® has been two approved uses in HER2-positive metastatic breast cancer (mBC):

- HERCEPTIN® in combination with the chemotherapy capecitabine for previously untreated HER2-positive mBC.
- HERCEPTIN® alone for HER2-positive mBC in people who have received one or more chemotherapies for mBC.

IMPORTANT SAFETY INFORMATION

HOW HERCEPTIN IS BELIEVED TO WORK

1. Trastuzumab (HERCEPTIN) blocks HER2 receptors on the surface of the cancer cells, which is a HER2-positive cell.
2. Trastuzumab (HERCEPTIN) antibody binds to HER2 receptors on the HER2-positive cancer cell.
3. Trastuzumab (HERCEPTIN) may also signal the body’s immune system to destroy the cancer cells.

Serious Side Effects and Additional 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-stage) breast cancer trial from significantly weakened heart muscle. The risk and seriousness of these heart problems were highest in patients 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 multigated acquisition (MUGA) scan. Some early-stage 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), and 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 six 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 cancer is HER2 positive before using Herceptin, as benefit has only been shown in patients who 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, feeling tired, shortness of breath, rash, low white and red blood cells, and muscle pain.

Because everyone is different, it is not possible to predict what side effects any one patient will have. Patients with questions or concerns about side effects should talk to their doctor.

Patients may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. Patients may also report side effects to Genentech at (888) 835-2555.

Patients should read the Herceptin Full Prescribing Information including Boxed WARNINGS, at http://www.herceptin.com.
Patients with questions or concerns about side effects should talk to their doctor. Because everyone is different, it is not possible to predict what side effects any one patient will have.

Herceptin, as benefit has only been shown in patients who are HER2-positive. Worsening of low white blood cell counts associated with chemotherapy has also occurred. Nursing mothers treated with Herceptin should discontinue nursing or discontinue Herceptin. 

Some patients have had serious infusion reactions and lung problems; fatal infusion reactions have been reported. Methods during Herceptin treatment and for at least six months after treatment with Herceptin.

Important Safety Information

- Because side effects from this treatment are common, it is important to know what side effects may happen and what symptoms patients should watch for:
  - A patient’s doctor may stop treatment if serious side effects happen. Patients must contact their healthcare team right away if they have questions or are worried about any side effects.

Most Serious Side Effect of Perjeta

Receiving Perjeta during pregnancy can result in the death of an unborn baby and birth defects. Birth control should be used while receiving Perjeta and for six months after a patient’s last dose of Perjeta. Patients who are breastfeeding should talk with their doctor about either stopping breastfeeding or stopping treatment with Perjeta.

- If a patient thinks she may be pregnant, she should contact her healthcare provider immediately.
- If a patient is exposed to Perjeta during pregnancy, she is encouraged to enroll in the MoHER Pregnancy Registry by contacting (800) 690-6720.

Other Possible Serious Side Effects

- Heart problems: Perjeta can result in heart problems, including those without symptoms (such as reduced heart function) and those with symptoms (such as congestive heart failure). A patient’s doctor may run tests to monitor the patient’s heart function before and during treatment with Perjeta.

- Infusion-related reactions: Perjeta is a medicine that is delivered into a vein through a needle. This process can cause reactions known as infusion-related reactions. The most common infusion-related reactions when receiving Perjeta, Herceptin, and docetaxel chemotherapy were feeling tired, abnormal or altered taste, allergic reactions, muscle pain and vomiting.

- Severe allergic reactions: Some people receiving Perjeta may have severe allergic reactions, called hypersensitivity reactions or anaphylaxis. This reaction may be severe, may happen quickly and may affect many areas of the body. Perjeta has been shown to work only in people with HER2-positive breast cancer. Patients must have a HER2 test to know if their breast cancer is HER2-positive before receiving an anti-HER2 treatment, such as Perjeta.

Most Common Side Effects

The most common side effects of Perjeta when given with Herceptin and docetaxel chemotherapy are:

- Diarrhea
- Hair loss
- Low levels of white blood cells with or without a fever
- Nausea
- Feeling tired
- Rash
- Damage to the nerves (numbness, tingling, pain in hands/feet)

Patients are encouraged to report side effects to Genentech and the FDA. They may report side effects to the FDA at (800) FDA 1088 or www.fda.gov/medwatch. They may also report side effects to Genentech at (888) 835-2555.
Kadcyla is not the same medicine as Herceptin. There are possible serious side effects of Kadcyla. Patients must contact their doctor right away if they experience any of these symptoms. The patient’s doctor may stop or lower the dose if the patient experiences any of these side effects.

Liver Problems
- Kadcyla may cause severe liver problems that can be life-threatening. Symptoms of liver problems may include: nausea, vomiting, diarrhea, fever, jaundice.

Heart Problems
- Kadcyla may cause heart problems, including those without symptoms (such as reduced heart function) and those with symptoms (such as congestive heart failure). Symptoms may include: shortness of breath, swelling of the ankles or legs, weakness or breathlessness.

Pregnancy
- Women who could become pregnant need to use effective birth control if they experience any of these symptoms. The patient’s doctor may do tests before starting Kadcyla.

Some early-stage breast cancer patients may also need to have a test done after they have been treated for their early-stage cancer. This includes a review of the patient’s health history and tests to see how well the heart is working. An abnormal test may indicate weak heart function before treatment begins. The patient’s doctor may do tests before starting Kadcyla.

Kadcyla is approved for the treatment of patients with HER2-positive metastatic breast cancer (mBC) who have received prior treatment including trastuzumab (Herceptin). Kadcyla is recommended for the treatment of HER2-positive mBC patients who:

- Have already been treated with taxane chemotherapy, or
- Have had their early-stage cancer come back during or within six months after they completed a course of treatment following surgery.

Additional Possible Serious Side Effects of Kadcyla

Lung Problems
- Kadcyla may cause lung problems, including inflammation of the lung tissue, which can be life-threatening. Symptoms of lung problems may include: trouble breathing, cough, shortness of breath and fluid in the lungs.

Infusion-Related Reactions
- Symptoms of an infusion-related reaction may include: fever or chills, skin rash, shortness of breath, wheezing, nausea, vomiting, diarrhea.

Nerve Damage
- Symptoms may include numbness and tingling, burning, or sharp pain, sensitivity to touch, lack of coordination, or muscle weakness.

Skin Reactions Around the Infusion Site
- Kadcyla may cause skin reddening, itching, pain or swelling during or within 24 hours of the infusion.

HER2 Testing and Kadcyla
- Patients must have a HER2 test to determine if their cancer is HER2-positive before taking Kadcyla. Kadcyla is only effective in people with HER2-positive cancer.

Common Side Effects of Kadcyla

In clinical studies, the most common side effects were: numbness, tingling, burning, or sharp pain, sensitivity to touch, weakness or loss of muscle function.

For full Prescribing Information and Boxed WARNINGS on Kadcyla, please visit http://www.kadcyla.com.