Genentech BIOONCOLOGY™

FACT SHEET

Media:	Krysta Pellegrino	(650) 467-6800
Investor:	Diane Schrick	(650) 225-1599
Advocacy:	Sonali Padhi	(650) 467-0842

Herceptin® (trastuzumab) Plus Chemotherapy in HER2-positive Metastatic Stomach (Gastric) Cancer Fact Sheet

In October 2010, the U.S. Food and Drug Administration (FDA) approved Herceptin 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.[1]

Herceptin is a targeted medicine (not a chemotherapy) designed to specifically block the HER2 protein on the surface of some cancer cells.[2] 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.[2]

The First Targeted Medicine for HER2-positive Metastatic Stomach Cancer

In the past 15 years, little progress has been made in the treatment of metastatic stomach cancer.[3] Based on people screened for HER2 status in the international Phase III ToGA (Trastuzumab for Gastric Cancer) study, approximately 22 percent of people with advanced stomach cancer are HER2 positive.[4] This approval is a step toward helping some people with HER2-positive metastatic stomach cancer live longer.

People diagnosed with metastatic stomach cancer should have the HER2 status of their tumor determined with FDA-approved diagnostic tests, as only people with HER2-positive disease are eligible for treatment with Herceptin plus chemotherapy.[4]

Herceptin Clinical Study in HER2-positive Metastatic Stomach Cancer

- The approval was based on the ToGA study, which showed people who received Herceptin plus chemotherapy lived longer compared to people who received chemotherapy alone.

- In the ToGA study, 594 people with locally advanced or metastatic, HER2-positive stomach cancer were randomized to receive Herceptin plus chemotherapy (cisplatin plus either capecitabine or 5-fluorouracil) or chemotherapy alone.
  - Results from the final overall survival (OS) analysis demonstrated Herceptin plus chemotherapy improved OS by 37 percent compared to chemotherapy alone (based on HR=0.73, 95 percent CI 0.60-0.91; median OS 13.5 vs. 11.0 months).
  - An updated OS analysis based on an additional year of follow-up showed a 25 percent improvement in OS (based on HR=0.80, 95 percent CI 0.67-0.97; median OS 13.1 vs. 11.7 months).
- All people in this trial had the HER2 status of their tumor cells determined using diagnostics developed by Dako.
- In the metastatic gastric cancer setting, the most common adverse reactions (≥ 10%) that were increased (≥ 5% difference) in the Herceptin arm as compared to the chemotherapy alone arm were neutropenia, diarrhea, fatigue, anemia, stomatitis, weight loss, upper respiratory tract infections, fever, thrombocytopenia, mucosal inflammation, nasopharyngitis, and dysgeusia. The most common adverse reactions which resulted in discontinuation of treatment on the Herceptin-containing arm in the absence of disease progression were infection, diarrhea, and febrile neutropenia.

About Herceptin

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.

Boxed WARNINGS 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) 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

[1] Herceptin [package insert]. South San Francisco, Calif.: Genentech, Inc. 2010.
[2] Valabrega D, et al. Trastuzumab: Mechanism Of Action, Resistance And Future Perspectives In HER2-Overexpressing Breast Cancer. *Annals of Oncology*. 2007;18: 977-984.
[3] Moiseyenko VM, et al. Randomized controlled phase III trial (TAX 325) comparing docetaxel (T) combined with cisplatin (C) and 5-flourouracil (F) to CF in patients with metastatic gastric adenocarcinoma (MGC). *J Clin Oncol,* 2005 ASCO Meeting Proceedings; 23:16s (suppl; abstr 4002).
[4] Bang Y, et al. Pathological features of advanced gastric cancer (GC): Relationship to human epidermal growth factor receptor 2 (HER2) positivity in the global screening programme of the ToGA trial. *J Clin Oncol*, 2009 ASCO Meeting Proceedings; 27:15s (suppl; abstr 4556).

HER0000093101