

Basel, 28 January 2010

Herceptin now approved in the EU for patients with HER2-positive advanced stomach cancer

First targeted biological therapy to show survival benefit in stomach cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the European Commission has approved Herceptin (trastuzumab) in combination with chemotherapy for use in patients with HER2-positive metastatic stomach (gastric) cancer. The approval is based on the impressive results from the international ToGA trial, which showed that treatment with Herceptin significantly prolongs the lives of patients with this aggressive cancer. Overall survival for patients with high levels of HER2 in the ToGA study was 16 months versus 11.8 months (on average) for patients receiving chemotherapy alone.ⁱ

“Herceptin is the first targeted biological therapy to show a survival benefit in advanced stomach cancer and represents a significant advance in the treatment of this devastating disease”, said Pascal Soriot, Chief Operating Officer (COO), Roche Pharmaceutical Division. “We believe that Herceptin will help patients with HER2-positive stomach cancer, as much as it has helped so many women with HER2-positive breast cancer.”

Based on the strong results from the phase III ToGA study, the submission for the label extension was reviewed in an accelerated process by the European Health Authorities, allowing patients to benefit sooner from this life-extending treatment. This marketing authorisation is valid with immediate effect in all European Union (EU) and EEA-EFTA states (Iceland, Liechtenstein and Norway). Following approval in the European Union, approvals for a label extension for Herceptin in other regions of the world are expected to follow soon.

“I am delighted that today’s approval will make Herceptin available to patients with HER-2 positive metastatic stomach cancer across Europe,” said Professor Eric Van Cutsem, University Hospital Gasthuisberg, Leuven, Belgium, one of the lead investigators of the ToGA trial. “The approval of Herceptin for HER2-positive stomach cancer represents an important advance for the treatment of these patients. Clinicians will need to ensure that patients with metastatic stomach cancer are accurately tested for HER2 expression.”

Stomach cancer is the second most common cause of cancer-related death in the world and is the fourth most commonly diagnosed cancer, with over 1,000,000 cases of stomach cancer diagnosed each year.ⁱⁱ Advanced stomach cancer is associated with a poor prognosis; the median survival time after diagnosis is approximately 10-11 months with currently available therapies.ⁱⁱⁱ Approximately 15 - 18% of stomach tumours show high levels of HER2^{iv,v} Early diagnosis of this disease is challenging because most patients do not show symptoms in the early stage.

About ToGA

ToGA is the first randomised Phase III trial investigating the use of Herceptin in patients with inoperable locally advanced, recurrent and/or metastatic HER2-positive stomach cancer. Approximately 3,800 patients were tested for HER2-positive tumours and 594 patients with HER2-positive disease were enrolled into the study. The rationale for conducting this trial was based on the knowledge that the targeted therapy Herceptin has demonstrated unprecedented efficacy in the treatment of HER2-positive breast cancer. In addition, the overexpression of HER2 was also observed in stomach cancer. Targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules involved in tumour growth and progression.

In the ToGA study, patients were randomised to receive one of the following regimens as their first line of treatment:

- A fluoropyrimidine (Xeloda or intravenous 5-FU) and cisplatin every 3 weeks for 6 cycles. Most patients were receiving Xeloda and cisplatin as chemotherapy
- Herceptin 6mg/kg every 3 weeks until progression in combination with a fluoropyrimidine and cisplatin for 6 cycles

The primary objective of the study was to demonstrate superiority in overall survival of the Herceptin-containing treatment arm compared to the chemotherapy alone arm. The pre-planned interim analysis was triggered by the occurrence of 347 events. Secondary endpoints for the study included progression-free survival, overall response rate, duration of response, safety and quality of life. In the ToGA study, no new or unexpected side effects were observed. For overall survival, the Hazard Ratio was 0.74 (CI 0.60, 0.91) with a highly significant p-value of p=0,0046. Herceptin increased the median overall survival time by 2.7 months to 13.8 months (intent to treat patient group, defined as IHC3+ or FISH-positive, represented 22% of patients tested for HER2 in the ToGA study). The response rate was increased with Herceptin from 34.5 % to 47.3%. Patients with tumours exhibiting high levels of HER2 (IHC3+ or IHC2+/FISH-positive, 16% of patients

tested for HER2 in the ToGA study) experienced even greater benefit from the addition of Herceptin. For these patients, overall survival in the study was 16 months on average versus 11.8 months for patients receiving chemotherapy alone. The EU label recommends Herceptin for patients expressing high levels of HER2.

About Herceptin

Herceptin is a humanised antibody, designed to target and block the function of HER2, a protein produced by a specific gene with cancer-causing potential. The mode of action of Herceptin is unique in that it activates the body's immune system and suppresses HER2 to target and destroy the tumour. Herceptin has demonstrated unprecedented efficacy in treating both early and advanced (metastatic) HER2-positive breast cancer. Given on its own as monotherapy as well as in combination with or following standard chemotherapy, Herceptin has been shown to improve response rates, disease-free survival and overall survival while maintaining quality of life in women with HER2-positive breast cancer.

Herceptin is marketed in the United States by Genentech, in Japan by Chugai and internationally by Roche. Since 1998, Herceptin has been used to treat more than 740,000 patients with HER2-positive breast cancer worldwide.

About Xeloda

Xeloda (capecitabine) is a highly effective targeted oral chemotherapy offering patients a survival advantage when taken on its own or in combination with other anticancer drugs. Xeloda uniquely activates the cancer-killing agent 5-FU (5-fluorouracil) directly inside the cancer cells so avoiding damage to healthy cells. Xeloda tablets can be taken by patients in their own home, reducing the number of hospital visits.

Licensed and marketed by Roche in more than 100 countries worldwide, Xeloda has more than ten years of proven clinical experience providing an effective and flexible treatment option to over 1.8 million people with cancer. Xeloda is currently approved in metastatic colorectal, breast and pancreatic cancer; advanced gastric cancer and adjuvant colon cancer.

Roche Personalised Healthcare: Fitting treatments to patients

Different people respond differently to medicines. The aim of Roche Personalised Healthcare (PHC) is to target treatments to the patients most likely to benefit. This means tailoring treatments to specific patient sub-groups who share similar characteristics in their genetic makeup or in the molecular nature of their

disease. This approach has enormous potential to make healthcare better, safer and more effective, with benefits for patients, physicians, payers, and society at large.

Herceptin treatment in breast cancer is a case in point: Measuring the levels of the protein HER2 in breast cancer cells with specific tests such as the assays from Roche Tissue Diagnostics (Ventana) reliably identifies patients who are likely to respond to Herceptin, a medicine that specifically targets HER2. Roche is also applying this approach to the diagnosis and the treatment of HER2-positive metastatic gastric cancer with Herceptin.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2008, Roche had over 80'000 employees worldwide and invested almost 9 billion Swiss francs in R&D. The Group posted sales of 45.6 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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