

Basel, 24 September 2009

Herceptin provides impressive survival benefit for patients with high levels of HER2 in their stomach cancer

Herceptin filed in Europe for treatment in HER2-positive advanced gastric cancer based on ToGA study results

A detailed analysis of the Phase III ToGA study announced today revealed an unprecedented survival benefit for patients whose tumours exhibited a particularly high level of HER2 when Herceptin (trastuzumab) was added to standard chemotherapy (Xeloda or intravenous 5-FU and cisplatin).

The analysis evaluated patient benefit according to the level of HER2 identified in their stomach tumour. Overall survival for patients with high levels of HER2 receiving Herceptin was 16 months on average versus 11.8 months for patients receiving chemotherapy alone.

These results were presented at the joint 15th Congress of the European Cancer Organisation (ECCO) and 34th Congress of the European Society for Medical Oncology (ESMO) in Berlin, Germany. They illustrate the importance of an individualized approach to patient care and the opportunity that a targeted medicine may offer.

“It is now clearly proven that Herceptin prolongs the lives of patients suffering from HER2-positive gastric cancer. As an investigator on this study and a treating physician, it is very rewarding to see a new effective treatment option emerging”, said principle investigator, Professor Eric Van Cutsem, University Hospital Gasthuisberg, Leuven, Belgium. “The results of the ToGA study reinforce the need for early and accurate HER2 testing of all advanced gastric cancer patients.”

Based on the significant findings of the ToGA study, Roche has submitted a label extension application with the EU Health Authorities for use of Herceptin in HER2-positive advanced gastric cancer. Applications for label extension in other regions of the world will follow as soon as possible.

“We are pleased to see the impressive benefit that the targeted therapy Herceptin provides for patients with

HER2-positive stomach cancer. That this benefit is even greater in patients with higher levels of HER2 demonstrates the significant advances through personalized medicine”, commented William M. Burns, CEO of Roche’s Pharmaceuticals Division, “Herceptin will become the new standard of care and will make an important contribution to helping these patients.”

Stomach cancer is the second most common cause of cancer-related death worldwide with over 1,000,000 new cases diagnosed each year. Stomach cancer is associated with poor prognosis and early diagnosis is challenging because most patients do not show symptoms until the later stages. Around 16% of stomach tumours express high levels of HER2 (IHC 3+ or IHC2+/FISH+)ⁱ.

About the ToGA study

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 gastric 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 tumor growth and progression.ⁱⁱ

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 disease progression in combination with a fluoropyrimidine and cisplatin which was stopped after a maximum of 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 corresponding to a 26% reduction in the risk of death. All patients who were included the study to receive Herceptin had a median overall survival increase by 2.7 months to

13.8 months. The response rate was increased with Herceptin from 34.5 % to 47.3%. Patients with tumours exhibiting higher levels of HER2 experienced even greater benefit from the addition of Herceptin.

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 received approval for use in the European Union for advanced (metastatic) HER2-positive breast cancer in 2000, and for early HER2-positive breast cancer in 2006. In the advanced setting, Herceptin is now approved for use as a first-line therapy in combination with paclitaxel where anthracyclines are unsuitable, as first-line therapy in combination with docetaxel, and as a single agent in third-line therapy. It is also approved for use in combination with an aromatase inhibitor for the treatment of post-menopausal patients with HER2 and hormone receptor co-positive metastatic breast cancer. In the early setting, Herceptin is approved for use following standard (adjuvant) chemotherapy. Herceptin is not approved for use in stomach 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 650,000 patients with HER2-positive breast cancer worldwide.

About Xeloda (capecitabine)

Xeloda 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 is converted to the active cancer-killing agent 5-FU (5-fluorouracil) directly inside the cancer cells, thus reducing 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.

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.

All trademarks used or mentioned in this release are protected by law.

Further information:

- Backgrounder Oncology: www.roche.com/media_backgrounder/media_oncology.htm
- Roche at ASCO: <http://www.roche.com/media/events/med-asco2009.htm>
- About cancer: www.roche.com/cancer.htm
- B-Roll and visuals can be found at: www.thenewsmarket.com

Roche Group Media Office

Phone: +41 61 688 8888 / Email: basel.mediaoffice@roche.com

- Daniel Piller (Head)
- Alexander Klauser
- Nina Schwab-Hautzinger
- Martina Rupp
- Claudia Schmitt

References

ⁱ Bang YJ et al. ASCO 2008 (poster no. 4526)

ⁱⁱ <http://www.cancer.gov/cancertopics/factsheet/Therapy/targeted>