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## **Herceptin landmark study (ToGA) reveals unprecedented survival benefit in HER2-positive stomach cancer**

### **Targeted therapy with Herceptin set to become the standard of care in HER2-positive stomach cancer**

Data from the ToGA study presented today at the American Society for Clinical Oncology Annual Meeting in Orlando, Florida showed that adding Herceptin (trastuzumab) to standard chemotherapy (Xeloda or intravenous 5-FU and cisplatin) prolongs the lives of patients with this aggressive cancer on average by nearly three months to 13.8 months. Advanced stomach (gastric) cancer is associated with a poor prognosis; the median survival time after diagnosis is approximately 10 months with currently available therapies.<sup>i</sup>

The international phase III study also showed that Herceptin reduces the risk of death in patients with HER2-positive advanced and inoperable stomach cancer by 26% compared to patients not receiving Herceptin. Patients with tumours exhibiting high levels of HER2 experienced even greater benefit from the addition of Herceptin, their lives were extended to 16 months on average.

"To see this unprecedented survival benefit for patients with HER2-positive stomach cancer is enormously rewarding," said principle investigator Prof. Eric Van Cutsem, University Hospital Gasthuisberg, Leuven, Belgium. "There is a high unmet medical need in advanced stomach cancer. The data from the ToGA study show that targeted therapy with Herceptin delivers a major advance in this therapeutic area."

Stomach cancer is the second most common cause of cancer-related death in the world with over 1,000,000 new cases diagnosed each year. Early diagnosis is challenging because most patients do not show symptoms in the early stage. Approximately 22% of stomach tumours are HER2-positive<sup>ii</sup>. This rate is the same in Europe and in Asia, where stomach cancer is particularly frequent.

"Herceptin has brought significant benefit to women suffering from HER2-positive breast cancer. We are extremely pleased to see its impressive benefit extending to patients with stomach cancer" commented William M. Burns, CEO of Roche's Pharmaceuticals Division. "The targeted therapy Herceptin will become the new standard of care and we can make an important contribution in helping these patients live longer."

Herceptin is already well established as the foundation of care for patients with HER2-positive breast cancer and now, based on the ToGA results, Roche will seek regulatory approvals for the use of Herceptin in HER2-positive advanced gastric.

### **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. A targeted anti-cancer therapy is a type of medication that blocks the growth of cancer cells by interfering with specific molecules which cause a tumor to grow.

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. The response rate was increased with Herceptin from 34.5 % to 47.3%. Patients with tumours exhibiting high 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 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 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 nearly 600,000 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 Cancer
- Metastatic Breast Cancer
- Adjuvant Colon Cancer
- Advanced Gastric Cancer
- Metastatic Pancreatic 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](http://www.roche.com).

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## **Further information:**

- Backgrounder Oncology: [www.roche.com/media\\_backgrounder/media\\_oncology.htm](http://www.roche.com/media_backgrounder/media_oncology.htm)
- Roche at ASCO: <http://www.roche.com/media/events/med-asco2009.htm>
- Videoclips, of broadcast standard: [www.thenewsmarket.com](http://www.thenewsmarket.com)

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## **References**

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<sup>i</sup> Ohtsu A. J Gastroenterol 2008;43:256-264

<sup>ii</sup> Bang YJ et al. ASCO 2008 (poster no. 4526)