Media Release

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Final analysis of Phase III HERA trial confirmed one year of Herceptin treatment as standard of care in early-stage HER2-positive breast cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) and the Breast International Group (BIG) today announced final results from the Phase III HERA trial, which confirmed that one year of Herceptin(trastuzumab) treatment remains the standard of care for people with early-stage HER2-positive breast cancer. These data showed that there was no difference in the time women lived without their disease returning (disease-free survival) when they received Herceptin for two years versus one year, a secondary endpoint of the study. After a median follow-up of eight years, the improvements in disease-free survival and overall survival for women who received Herceptin for one year remained statistically significant compared to women who underwent observation alone. There were no new safety findings in the study.

"Herceptin has changed the lives of many people with HER2-positive early breast cancer by increasing their chance of cure. HERA is one of the largest and longest-running breast cancer trials and demonstrates our commitment to people with this aggressive disease," said Hal Barron, M.D., Roche's Chief Medical Officer and Head of Global Product Development. "These results answer an important question and support current medical practice, where Herceptin treatment for one year is recommended and approved for people with early-stage HER2-positive breast cancer."

"It's essential that our clinical trials help us understand just how long patients need to receive a particular treatment." said Dr Martine Piccart, Chair of BIG. "These results give us both the evidence and the reassurance that it's not necessary to give patients with early-stage HER2-positive breast cancer Herceptin for more than one year."

The HERA data will be presented in the Presidential Symposium II at the ESMO 2012 Congress (European Society for Medical Oncology) in Vienna, Austria by Richard D. Gelber, PhD, of the Dana-Farber Cancer

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Institute, Massachusetts, USA (Abstract #LBA6_PR, Monday 1 October, 16:15-16.30 CEST).[1] The HERA data will also be presented in the official ESMO press media briefing on Monday 1 October at 08.15-9.00 CEST.

Results from the HERA study were originally reported in 2005, when an interim analysis showed the study met its primary endpoint of a significant benefit in disease-free survival (HR=0.54, p≤0.0001) for women who received Herceptin for one year compared with observation. Based on data from HERA and three additional randomised trials (NSABP B-31, NCCTG N9831, BCIRG 006), involving more than 13,000 women overall,[2,3,4] Herceptin treatment for one year is approved by global regulatory authorities and recommended by international guidelines for people with early-stage HER2-positive breast cancer. To date, more than 1.2 million people worldwide have been treated with Herceptin.

HERA study results

These final results confirmed that one year of Herceptin treatment remains the standard of care for people with early-stage HER2-positive breast cancer. The results also showed that after a median follow-up of eight years, the improvements in disease-free survival and overall survival for women who received Herceptin remained statistically significant compared with observation:

Endpoint	One year Herceptin vs. observation*	One year vs. two years Herceptin**
Disease-free survival	• HR=0.76, p<0.0001 • 24% reduction in the risk of disease recurrence	• HR=0.99, p=0.86 • No difference
Overall survival	• HR=0.76, p=0.0005 • 24% reduction in the risk of death	• HR=1.05, p=0.63 • No difference

*Comparison based on intent to treat population. The observation arm includes women who crossed over to receive Herceptin treatment (more than 50 percent of women) following the release of the one year versus observation results after the interim analysis in 2005.

**Comparison based on population alive and disease free for at least 366 days following randomisation.

Safety profile

No new safety signals were observed in the study. Overall, the incidence of cardiac dysfunction in women remained low in all patients. There was a low incidence in all patients (less than or equal to one percent) of symptomatic congestive heart failure (CHF), a condition where the heart has lost the ability to pump blood around the tissues of the body (symptoms can include shortness of breath). In addition, there was a slightly higher incidence of certain adverse events among women who received Herceptin for two years compared

with one year or with observation alone:

- Reduction in left ventricular ejection fraction, or the amount of blood pumped out of the left ventricle of the heart (without symptoms or mild symptoms only) – at 7.2 percent, 4.1 percent and 0.9 percent for women receiving two years of Herceptin, one year of Herceptin or observation alone, respectively.
- Severe adverse events (grade ≥3) experienced by at least one patient in a treatment group – at 20.4 percent, 16.3 percent and 8.2 percent for those receiving two years of Herceptin, one year of Herceptin or observation alone, respectively.

About the HERA study

HERA (HERceptin Adjuvant) is a Phase III, international, open-label, multicentre trial conducted by BIG which included 5,102 women, who were randomised 1:1:1 to observation or to one year or two years of Herceptin treatment. Observation only was the standard of care at the time the HERA study was started. Women were enrolled at 480 sites in 39 countries worldwide and had all been diagnosed with early-stage HER2-positive breast cancer. All women had already received chemotherapy and radiotherapy (if applicable) before or after their breast cancer surgery. The HERA study allowed for a wide range of chemotherapy regimens to be used and both lymph node-positive and lymph node-negative participants were eligible for enrolment. The trial evaluated disease-free survival within the following study groups:

- Herceptin monotherapy for one year (given every three weeks) compared to observation (primary endpoint)
- Herceptin monotherapy for one year compared to Herceptin monotherapy for two years (secondary endpoint).

Other HERA trial endpoints include the time that women lived overall (overall survival), the time that women lived without relapse of their disease (relapse-free survival), the time that women lived with no sign of disease in a different part of the body from where it was originally treated (distant disease-free survival), time to disease recurrence, DFS of Herceptin given for two years compared to observation and the safety profile.

About breast cancer

Breast cancer is the most common cancer among women worldwide.[5] Each year about 1.4 million new cases of breast cancer are diagnosed worldwide, and over 450,000 women will die of the disease annually.[5]
In HER2-positive breast cancer, increased quantities of the human epidermal growth factor receptor 2 (HER2) are present on the surface of the tumour cells. This is known as “HER2 positivity” and affects

approximately 15-20 percent of women with breast cancer.[6] HER2-positive cancer is a particularly aggressive form of breast cancer.[4]

About Herceptin in breast cancer

Herceptin (trastuzumab) is a humanised monoclonal antibody, designed to target and block the function of HER2, a protein produced by a specific gene with cancer-causing potential when it is overexpressed. The mode of action of Herceptin is unique in that it activates the body's immune system and suppresses HER2 signalling 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 overall survival, response rates and disease-free 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 1.2 million people with HER2-positive cancer worldwide.

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 personalized healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2011, Roche had over 80,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 42.5 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.

About BIG

The Breast International Group (BIG) is a non-profit organisation for academic breast cancer research groups from around the world, based in Brussels, Belgium.

Founded by leading European opinion leaders in 1999, BIG now constitutes a network of 49 collaborative research groups based in Europe, Canada, Latin America, Asia and Australasia. These entities are tied to several thousand specialised hospitals and research centres worldwide. More than 30 clinical trials are run or

are under development under the BIG umbrella. BIG also works closely with the US National Cancer Institute (NCI) and the North American Breast Cancer Groups (NABCG), so that together they act as a strong integrating force in the breast cancer research arena.

To make significant scientific advances in breast cancer research, reduce unnecessary duplication of effort, and optimally serve those affected by the disease, large-scale cooperation is crucial. Therefore BIG facilitates breast cancer research at international level, by stimulating cooperation between its members and other academic networks, and collaborating with, but working independently from, the pharmaceutical industry. www.breastinternationalgroup.org

Additional information

Roche in Oncology: www.roche.com/de/media/media_backgrounder/media_oncology.htm

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