New data from Phase III EMILIA study showed Roche’s trastuzumab emtansine (T-DM1) significantly improved survival of people with HER2-positive metastatic breast cancer

Pivotal study met co-primary efficacy endpoint of overall survival

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced updated results from the Phase III EMILIA study, which showed that trastuzumab emtansine (T-DM1) significantly extended the lives (improved overall survival) of people with HER2-positive metastatic breast cancer (mBC) compared to the combination of lapatinib and Xeloda (capecitabine). The EMILIA study, in people with HER2-positive mBC who had previously received Herceptin (trastuzumab) and taxane chemotherapy, has now met both co-primary efficacy endpoints of significant improvements in overall survival and progression-free survival (PFS). These data will be presented at an upcoming medical meeting.

Genentech has submitted a Biologics License Application (BLA) for trastuzumab emtansine to the US Food and Drug Administration (FDA) and Roche will shortly be submitting a Marketing Authorisation Application to the European Medicines Agency (EMA).

“We are extremely pleased to announce that people treated with trastuzumab emtansine survived significantly longer than those who received a standard option for this aggressive advanced breast cancer,” said Hal Barron, M.D., Chief Medical Officer and Head, Global Product Development. “We believe that antibody-drug conjugates have the potential to change the future treatment of cancer, and we look forward to working with regulatory authorities in the hope of bringing another potential treatment option to people with HER2-positive metastatic breast cancer.”

Based on these updated overall survival results, people in the lapatinib and Xeloda arm of EMILIA will be offered the option to receive trastuzumab emtansine.

Trastuzumab emtansine is an antibody-drug conjugate (ADC) being studied in HER2-positive cancers. It is comprised of the antibody trastuzumab and the chemotherapy DM1 attached together using a stable linker.
Trastuzumab emtansine is designed to target and inhibit HER2 signalling and deliver the chemotherapy DM1 directly inside HER2-positive cancer cells. Roche has been researching the HER2 pathway for three decades. The development of HER2-targeted therapies represents one of the first successful examples of personalised healthcare.

**About the EMILIA study**

EMILIA (TDM4370g/BO21977) is an international, Phase III, randomised, open-label study comparing trastuzumab emtansine alone to lapatinib in combination with Xeloda in 991 people with HER2-positive locally advanced or metastatic breast cancer who had previously been treated with Herceptin and a taxane-based chemotherapy.

The co-primary efficacy endpoints of the study are PFS (as assessed by an independent review committee) and overall survival. Other study endpoints include one-year and two-year survival rates, safety profile, PFS as assessed by investigator, objective response rate, duration of response and quality of life.

**Updated EMILIA overall survival results**

This confirmatory analysis of overall survival in the Phase III EMILIA study crossed the pre-specified boundary that showed trastuzumab emtansine significantly extended the lives of people with HER2-positive mBC compared to the combination of lapatinib and Xeloda.

**Previously presented EMILIA results**

Results from the EMILIA study were presented at the 48th Annual Meeting of the American Society of Clinical Oncology (ASCO) in June 2012:

- There was a significant improvement in the time people receiving trastuzumab emtansine (n=495) lived without their disease getting worse (PFS) compared to those who received lapatinib plus Xeloda (n=496), as assessed by independent review.
- The risk of disease worsening was reduced by 35 percent for people who received trastuzumab emtansine compared to those who received lapatinib plus Xeloda (HR=0.65, p<0.0001; median PFS 9.6 months vs. 6.4 months, respectively).
- Fewer people who received trastuzumab emtansine experienced Grade 3 or higher (severe) adverse events (AEs) than those who received lapatinib plus Xeloda, at 40.8 percent compared to 57.0 percent, respectively. For people receiving trastuzumab emtansine, compared to those receiving lapatinib plus Xeloda, the most common (occurring in more than 2 percent of participants) Grade 3 or higher AEs were...
low platelet count (12.9 percent vs. 0.2 percent), increased levels of enzymes released by the liver and other organs (aspartate aminotransferase: 4.3 percent vs. 0.8 percent; alanine aminotransferase: 2.9 percent vs. 1.4 percent; in most people, these levels had returned to normal by the time of the next dose of trastuzumab emtansine), and anaemia (2.7 percent vs. 1.6 percent).

- A previous interim analysis of overall survival demonstrated a trend towards improved overall survival in people receiving trastuzumab emtansine compared to those who received lapatinib plus Xeloda. However, the data were not considered statistically significant at that time.

**About trastuzumab emtansine**

Trastuzumab emtansine is an antibody-drug conjugate (ADC) being studied in HER2-positive cancers. It is comprised of the antibody trastuzumab and the chemotherapy DM1 attached together using a stable linker. Trastuzumab emtansine has the mechanisms of action of both trastuzumab and DM1. Trastuzumab emtansine is designed to target and inhibit HER2 signalling and deliver the chemotherapy DM1 directly inside HER2-positive cancer cells. Trastuzumab emtansine binds to the HER2-positive cancer cells, and is thought to block out-of-control signals that make the cancer grow while also calling on the body's immune system to attack the cancer cells. Once trastuzumab emtansine is absorbed into those cancer cells, it is designed to destroy them by releasing the DM1.

Genentech, a member of the Roche Group, licenses technology for trastuzumab emtansine under an agreement with ImmunoGen, Inc.

Building on the results of trastuzumab emtansine studies to date, there are approximately 25 ADCs in Roche's pipeline.

**About breast cancer**

Breast cancer is the most common cancer among women worldwide. 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. 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. HER2-positive cancer is a particularly aggressive form of breast 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 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.

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Roche Group Media Relations
Phone: +41 61 688 8888 / e-mail: basel.mediaoffice@roche.com
- Alexander Klauser (Head)
- Silvia Dobry
- Daniel Grotzky

References
1. Blackwell K et al Primary results from EMILIA, a phase 3 study of trastuzumab emtansine (T-DM1) vs capecitabine (X) and lapatinib (L) in HER2-positive locally advanced or metastatic breast cancer (MBC) previously treated with trastuzumab (T) and a taxane. ASCO 2012 Abstract LBA1.