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CHUGAI
Roche Group

Translation

New Drug Application Filed for Anti-Cancer Agent "Pertuzumab" for the Treatment of HER2-Positive Metastatic or Recurrent Breast Cancer

May 25, 2012 (Tokyo) – Chugai Pharmaceutical Co., Ltd. [Main Office: Chuo-ku, Tokyo. Chairman & CEO: Osamu Nagayama (hereafter, "Chugai")] announced today that it has filed a new drug application to the Ministry of Health, Labour and Welfare (MHLW), for humanized HER dimerization inhibitory monoclonal antibody "pertuzumab" for the treatment of "HER2-positive metastatic or recurrent breast cancer."

Chugai filed an application for approval with the MHLW based on the results from a multinational phase III clinical trial (CLEOPATRA trial, including Japanese patients) and a domestic phase I clinical trial.
The CLEOPATRA trial compared the combination of pertuzumab, trastuzumab (Herceptin®) and docetaxel to trastuzumab and docetaxel in patients with previously untreated HER2-positive metastatic breast cancer. Patients who received pertuzumab in combination with trastuzumab and docetaxel experienced a 38 percent reduction in the risk of their disease worsening or death (progression free survival; PFS) (hazard ratio=0.62; $p<0.0001$). The median PFS improved by 6.1 months from 12.4 months of trastuzumab and docetaxel to 18.5 months of pertuzumab, trastuzumab and docetaxel.
Adverse events were similar to those reported to date with trastuzumab and docetaxel, and there was no marked increase in adverse events by the combination of pertuzumab.

The number of patients newly diagnosed as breast cancer in Japan continues to rise each year and is estimated to exceed 48,000 women in 2015*. As the top pharmaceutical company in the field of oncology, Chugai will work for the approval to provide patients and medical professionals with new treatment options as soon as possible.

*A. Oshima, T. Kuroishi, K. Tajima, Cancer White Paper - Incidence / Death / Prognosis - 2004, Shinoharashinsha Inc.

About pertuzumab

Pertuzumab is a humanized monoclonal antibody developed by Roche for the treatment of breast cancer, that targets HER2 as in a complementary way to trastuzumab. Roche is the leading company in the world working on personalised healthcare medicines from the early period. In HER2-positive breast cancer patients, HER2 exists in large amount on the surface of cancer cells and sends out proliferation signals to cells. Trastuzumab works by binding to HER2 to suppress its activity. Pertuzumab works by binding to HER2 to prevent HER2 from making pairs with HER3 or other types of HER. which also sends proliferation signals when making pairs with HER2. In addition, pertuzumab and trastuzumab binding to HER2 draw immune cells (macrophage or NK cells) to attack and kill cancer cells by the activation of antibody dependent cellular cytotoxicity.

New drug applications for pertuzumab for people with previously untreated, HER2-positive metastatic cancer have been submitted to the U.S Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

About efforts for making personalised healthcare targeting HER2

Trastuzumab is a personalised healthcare medicine realized and developed first in the world by Roche.

There is a type of breast cancer in which a protein called HER2 is overexpressed. Trastuzumab is a drug developed to target HER2, and therefore it is effective for this type of breast cancer. In Japan, HER2 testing has become a common practice, and is performed in about 90% of patients with breast cancer. Pertuzumab also targets HER2. HER2 testing is performed before drug administration in order to determine whether or not the drug may be effective. By doing so, one can avoid administering the drug to patients who have breast cancer without HER2 expression, in whom the drug will probably not work.

Chugai is also conducting clinical development of a compound T-DM1, an antibody-drug conjugate which also targets HER2.

Mode of action of pertuzumab (simplified diagram)