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CHUGAI
Roche Group

Translation

First HER2 targeted Antibody Drug Conjugate "Kadcyla®," an Anti-Cancer Agent, Approved for HER2-positive Inoperable or Recurrent Breast Cancer

September 20, 2013 (Tokyo) – Chugai Pharmaceutical Co., Ltd. [Main Office: Chuo-ku, Tokyo. Chairman & CEO: Osamu Nagayama (hereafter, "Chugai")] announced today that it obtained approval by the Japanese Ministry of Health, Labour and Welfare (MHLW) on September 20, 2013, for "HER2-positive inoperable or recurrent breast cancer," for the HER2 targeted anti-body drug conjugate, "Kadcyla® Intravenous Infusion 100 mg and 160 mg" [generic name: trastuzumab emtansine (genetical recombination)] (hereafter, Kadcyla®).

In January 2013, Chugai filed a new drug application for approval for HER2-positive inoperable or recurrent breast cancer based on results from a Japanese phase II clinical trial and a global phase III clinical trial (The EMILIA trial). This approval was obtained based on data from these clinical trials.

The EMILIA trial is an international phase III study comparing Kadcyla® alone to lapatinib in combination with capecitabine in patients with HER2-positive metastatic or unresectable locally advanced breast cancer who had previously been treated with trastuzumab (Herceptin®) and a taxane. Patients from Japan were not included in this trial.

Progression free survival (PFS) was one of its primary endpoints, and patients who received Kadcyla® experienced a 35 percent reduction in the risk of disease progression or death compared to those who received lapatinib plus capecitabine. The median PFS improved by 3.2 months from 6.4 months on lapatinib and capecitabine to 9.6 months on Kadcyla® (hazard ratio=0.65; $p<0.0001$).

As for overall survival (OS), another primary endpoint, the risk of death was reduced by 32% for patients who received Kadcyla® compared to those who received lapatinib plus capecitabine. Patients in the study treated with Kadcyla® survived a median time of 5.8 months longer than those who received lapatinib and capecitabine (median OS: 30.9 months vs. 25.1 months) (hazard ratio=0.68; p=0.0006).

Regarding safety, 40.8 percent of the patients who received Kadcyla® and 57.0 percent of the patients who received lapatinib plus capecitabine experienced Grade 3 or higher AEs. The most common Grade 3 or higher AEs reported in patients receiving Kadcyla®, compared to those receiving lapatinib plus capecitabine, included low platelet count and increase of AST and ALT levels.

The phase II trial conducted in Japan confirmed the efficacy and the tolerability of Kadcyla® in Japanese patients with HER2-positive metastatic or unresectable locally advanced breast cancer.
The number of patients newly diagnosed with breast cancer in Japan has been continuing to rise each year and is estimated to become approximately 60,000 during 2015-2019 on annual average.* Overexpression of HER2 has been observed in approximately 20 percent of breast cancer patients.

As the top pharmaceutical company in the field of oncology, Chugai is convinced that Kadcyla® can contribute to the treatment of patients with "HER2-positive inoperable or recurrent breast cancer" by providing a new therapeutic option.

* T. Sobue, et al., Cancer White Paper 2012, Shinoharashinsha Inc.

About Kadcyla® [trastuzumab emtansine (T-DM1)]

Kadcyla® is an anti-body drug conjugate. It comprises of the anit-HER2 humanized monoclonal antibody, trastuzumab, and a chemotherapeutic drug, DM1, attached together using a stable linker. Kadcyla® is designed to target HER2, inhibit HER2 signaling, induce antibody-dependent cell mediated cytotoxicity, and deliver the chemotherapeutic drug DM1 directly inside HER2-positive cancer cells. Once Kadcyla® is taken up by those cancer cells, it is designed to destroy them by the DM1.
Kadcyla® was approved for patients with previously treated, HER2-positive metastatic breast cancer in the US in February 2013 and a Marketing Authorisation Application has been submitted to the European Medicines Agency (EMA) by Roche.

Roche licenses technology for Kadcyla® under an agreement with ImmunoGen, Inc.

About efforts for making personalised healthcare targeting HER2

Roche is the leading company in the world working on personalised healthcare medicines. Herceptin® is a personalised healthcare medicine realized and developed first in the world by Roche. In Japan, Herceptin® was approved in 2001 and has been widely used in the treatment of patients with HER2-positive breast cancer.
There is a type of breast cancer in which a protein called HER2 is overexpressed. Herceptin® is designed 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 percent of patients with breast cancer. Kadcyla® 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.
As a new drug that targets HER2, Chugai has launched HER2 dimerization inhibitory monoclonal antibody, "Perjeta® I.V. Infusion 420mg/14mL" in September 2013.