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Chugai Files New Drug Application in Japan for Fixed-Dose Subcutaneous Combination of Pertuzumab and Trastuzumab for HER2-Positive Breast and Colorectal Cancer

- Chugai files a new drug application for fixed-dose subcutaneous combination of pertuzumab and trastuzumab (same monoclonal antibodies as in Perjeta and Herceptin) in Japan
- The application is based on data including the results from the global phase III FeDeriCa study in patients with HER2-positive breast cancer

TOKYO, September 29, 2022 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that it filed a new drug application for RG6264 today with the Ministry of Health, Labour and Welfare (MHLW) for the treatment of HER2-positive breast cancer, and HER2-positive colorectal cancer that has progressed after chemotherapy. RG6264 is a fixed-dose subcutaneous combination of antineoplastic agent / anti-HER2 humanized monoclonal antibody, Perjeta® [generic name: pertuzumab (genetical recombination)] and anti-HER2 humanized monoclonal antibody / antineoplastic agent, Herceptin® [generic name: trastuzumab (genetical recombination)].

The fixed-dose subcutaneous combination contains the same monoclonal antibodies as Perjeta, Herceptin, and vorhyaluronidase alfa (genetical recombination) in a single vial. Hyaluronidase, an enzyme that breaks down hyaluronic acid, is considered to increase dispersion and absorption of the antibodies. It takes 150 minutes for a sequential infusion of a loading dose of Herceptin and Perjeta using intravenous formulations, excluding follow-up observation, and 60-150 minutes for maintenance infusions.[1,2,3] By comparison, in FeDeriCa study it took approximately eight minutes to infuse a loading dose of RG6264 and five minutes for maintenance infusions. The safety of RG6264 shown in FeDeriCa study was comparable to the intravenous administration of Perjeta and Herceptin. In the study, alopecia, nausea, diarrhea, and anemia were reported as adverse events.[4] Another clinical study (PHranceSCa study) showed that 85% of patients (N=136/160) evaluated in the study preferred RG6264 injection to the separate IV administration of Perjeta and Herceptin.[5]

“We are very pleased that the regulatory application has been filed for the subcutaneous formulation of the combination therapy of Perjeta and Herceptin, the standard therapy for HER2-positive breast cancer,” said Chugai's President and CEO, Dr. Osamu Okuda. “Reduction of administration time is expected to offer better convenience for patients and to reduce the burden on healthcare professionals. In order to deliver new value to patients and healthcare professionals as soon as possible, we will work together with Roche to obtain approval.”

The application is based on the results of the global phase III FeDeriCa study and an overseas phase II PHranceSCa study. FeDeriCa study evaluated the pharmacokinetics, efficacy, and safety of RG6264 with

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patients with HER2-positive breast cancer. PHranceSCa study examined patient preference and satisfaction with subcutaneous administration of RG6264 in HER2-positive breast cancer. Chugai is responsible for the development of RG6264 in Japan and has been participating in FeDeriCa study.

[Reference information]

Roche's fixed-dose subcutaneous combination of Perjeta and Herceptin comparable to intravenous formulations in people with HER2-positive breast cancer (Press release issued by Roche on December 12, 2019)

https://www.roche.com/media/releases/med-cor-2019-12-12

About FeDeriCa study[4)]

FeDeriCa is an international, multi-center, two-arm, randomized, open-label, phase III study evaluating the pharmacokinetics, efficacy and safety of subcutaneous injection of the fixed-dose combination of Perjeta and Herceptin in combination with chemotherapy, compared with standard intravenous infusions of Perjeta and Herceptin in combination with chemotherapy in 500 people with HER2-positive early breast cancer who are being treated in the neoadjuvant (before surgery) and adjuvant (after surgery) settings. The primary endpoint of the study is minimum levels of Perjeta in the blood during a given dosing interval (C_{trough}). Secondary endpoints include safety; minimum levels of Herceptin in the blood during a given dosing interval (C_{trough}); and pathological complete response (pCR) in the breast and axilla.

About PHranceSCa study[5)]

PHranceSCa is an overseas phase II randomized clinical study to evaluate patient preference and satisfaction for the fixed-dose combination of Perjeta and Herceptin for subcutaneous injection in 140 patients with HER2-positive early breast cancer. The primary endpoint is patient's preference for this drug based on responses to the Patient Preference Questionnaire (PPQ). Secondary endpoints include patient satisfaction with this drug and Perjeta and Herceptin intravenous formulations as measured by the Therapy Administration Satisfaction Questionnaire (TASQ), and patient's selection of this drug during continued treatment.

About Perjeta

Perjeta is a humanized monoclonal antibody that targets human epidermal growth factor receptor type 2 (HER2), which is involved in the growth of tumor cells. Perjeta in combination with Herceptin blocks the HER-signaling system more extensively. The drug was launched in 2013 for "inoperable or recurrent HER2-positive breast cancer." The indication was amended as "HER-2 positive breast cancer," after obtaining regulatory approval for the additional indication of "neoadjuvant and adjuvant therapy in HER2-positive breast cancer" in 2018. In addition, it was approved for the indication of "advanced or recurrent HER2-positive colon cancer or rectal cancer not amenable to curative resection that has progressed after cancer chemotherapy" in 2022.

About Herceptin

Herceptin, like Perjeta, is a humanized monoclonal antibody that targets human epidermal growth factor receptor type 2 (HER2), which is involved in the growth of tumor cells. Herceptin was launched in 2001 for "metastatic breast cancer overexpressing HER2." Thereafter, the indication was changed to "Breast

cancer overexpressing HER2" in 2011 based on the approved postoperative drug therapy and the additional approval of preoperative drug therapy based on a public knowledge-based application. In 2011, it was approved for the treatment of patients with "advanced or recurrent gastric cancer overexpressing HER2 not amenable to curative resection", in 2021 for "advanced or recurrent HER2-positive salivary gland cancer not amenable to curative resection" and in 2022 for "advanced or recurrent HER2-positive colon cancer or rectal cancer not amenable to curative resection that has progressed after cancer chemotherapy."

Sources

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5. European Journal of Cancer. Preference for the fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injection in patients with HER2-positive early breast cancer (PHranceSCa): A randomised, open-label phase II study. Available from: https://www.sciencedirect.com/science/article/pii/S0959804921002148?via%3Dihub (Accessed in September 2022)

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