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Chugai Obtains Regulatory Approval for Phesgo, the Fixed-Dose Subcutaneous Combination of Perjeta and Herceptin for HER2-Positive Breast and Colorectal Cancer

- Phesgo is a fixed-dose combination of pertuzumab and trastuzumab (the monoclonal antibodies contained in Perjeta and Herceptin), which are used in HER2-positive breast and colorectal cancer
- This is a subcutaneous formulation that can be administered over 5-8 minutes, compared to the intravenous infusion, which is administered over 60-150 minutes

TOKYO, September 25, 2023 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that it has obtained regulatory approval today from the Ministry of Health, Labour and Welfare (MHLW) for Phesgo® combination for Subcutaneous Injection MA, IN [generic name: pertuzumab (genetical recombination), trastuzumab (genetical recombination) and vorhyaluronidase alfa (genetical recombination)] (hereafter, Phesgo), antineoplastic agent / anti-HER2 humanized monoclonal antibody for the treatment of "HER2-positive breast cancer" and "Advanced or recurrent HER2-positive colorectal cancer that has progressed following cancer chemotherapy and is not amenable to curative resection."

"We are pleased to have obtained approval in Japan for Phesgo, a fixed-dose combination for subcutaneous use containing the same anti-HER2 agents of Perjeta® and Herceptin®, the standard therapy for HER2-positive breast cancer. Reducing administration time is expected to improve convenience for patients and reduce the burden on healthcare system and professionals. We are preparing for the launch of this drug so that it can be used for treatment as soon as possible," said Dr. Osamu Okuda, Chugai's President and CEO.

This subcutaneous fixed-dose combination without preparation contains the same monoclonal antibodies as Perjeta and Herceptin, and also a vorhyaluronidase alfa (genetical recombination) combined in a single vial. It takes over eight minutes for a loading dose of Phesgo and over five minutes for the subsequent doses. By comparison, it takes 150 minutes for a sequential infusion of a loading dose of Perjeta and Herceptin using intravenous formulations (excluding follow-up observation), and 60-150* minutes for the subsequent maintenance dose infusions.[1,2,3)]

*Both drugs can be shortened to 30 minutes if the initial administration is well tolerated

This approval is based on the results of the global phase III FeDeriCa study including Japan and an overseas phase II PHranceSCa study. FeDeriCa study evaluated the pharmacokinetics, efficacy, and safety of Phesgo with patients with HER2-positive breast cancer. PHranceSCa study examined patient preference and satisfaction with subcutaneous administration of Phesgo in HER2-positive breast cancer. Chugai is responsible for the development of Phesgo in Japan and has been participating in FeDeriCa study.

CHUGAI PHARMACEUTICAL CO., LTD. Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome, Chuo-ku Tokyo, 103-8324 Japan
Media Relations Group TEL:+81-(0)3-3273-0881 E-mail:pr@chugai-pharm.co.jp
Investor Relations Group TEL:+81-(0)3-3273-0554 E-mail:ir@chugai-pharm.co.jp

The FeDeriCa study validated the non-inferiority (pharmacokinetics) of blood concentration of Perjeta between Phesgo and intravenous formulations of Perjeta and Herceptin (primary endpoint). The most common adverse events were alopecia (77% in the Phesgo group and 70% in the intravenous formulation group. The same order applies hereinafter), nausea (59%, 60%), diarrhea (58%, 55%), and anemia (34%, 41%) in the Phesgo group and the intravenous formulation group, respectively.[4)] In PHranceSCa study showed that 85% of patients (n=136/160) evaluated in the study preferred Phesgo, subcutaneous injection to the separate IV administration of Perjeta and Herceptin, citing less time in the clinic as the most common reason.[5)]

[Approval Information]
Product name: PHESGO® combination for Subcutaneous Injection MA, IN
Generic name: pertuzumab (genetical recombination), trastuzumab (genetical recombination) and vorhyaluronidase alfa (genetical recombination)
Indications:
· HER2-positive breast cancer
· Advanced or recurrent HER2-positive colorectal cancer that has progressed following cancer chemotherapy and is not amenable to curative resection
Dosage and administration:
< HER2-positive breast cancer >
The usual adult dosage is an initial dose of 1200 mg, 600 mg, and 30000 U of pertuzumab (genetical recombination), trastuzumab (genetical recombination), and vorhyaluronidase alfa (genetical recombination), respectively, administered subcutaneously over 8 minutes, followed by 600 mg, 600 mg, and 20000 U of the second and subsequent doses over 5 minutes every 3 weeks thereafter, in combination with other antineoplastic agents. For neoadjuvant or adjuvant therapy, the duration of treatment should be up to 12 months.
< Advanced or recurrent HER2-positive colorectal cancer that has progressed following cancer chemotherapy and is not amenable to curative resection >
The usual adult dosage is an initial dose of 1200 mg, 600 mg, and 30000 U of pertuzumab (genetical recombination), trastuzumab (genetical recombination), and vorhyaluronidase alfa (genetical recombination), respectively, administered subcutaneously over 8 minutes, followed by 600 mg, 600 mg, and 20000 U of the second and subsequent doses over 5 minutes every 3 weeks thereafter.

[Reference]
Chugai Files New Drug Application in Japan for Fixed-Dose Subcutaneous Combination of Pertuzumab and Trastuzumab for HER2-Positive Breast and Colorectal Cancer (Press release issued on September 29, 2022)
https://www.chugai-pharm.co.jp/english/news/detail/20220929170000_945.html

About Phesgo (Pertuzumab, Trastuzumab and vorhyaluronidase alfa)
Phesgo, 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

using Halozyme Therapeutics' Enhanze® drug delivery technology.[6] The monoclonal antibodies in Phesgo are identical to those in Perjeta and Herceptin. The mechanisms of action of Perjeta and Herceptin are believed to complement each other as both bind to the HER2 receptor, but in different locations.[7,8] The combination of Perjeta and Herceptin is thought to provide a more comprehensive, dual blockade of the HER signaling pathways.[7,8]

About FeDeriCa study[4]

FeDeriCa study 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 study 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 160 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.

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