

CHMP recommends EU approval of Roche's Phesgo (fixed-dose combination of Perjeta and Herceptin for subcutaneous injection) for HER2-positive breast cancer

- **Phesgo offers faster and less invasive delivery of standard of care treatment with Perjeta and Herceptin, under the skin in just minutes, compared to hours with intravenous infusion^{1,2,3}**
- **Subcutaneous administration is preferred by patients, physicians and healthcare providers, and can be associated with reduced hospital times and costs^{4,5,6}**
- **This is the first time that Roche has combined two monoclonal antibodies that can be administered by a single subcutaneous injection**

Basel, 13 November 2020 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended the approval of Phesgo®, a fixed-dose combination of Perjeta® (pertuzumab) and Herceptin® (trastuzumab) with hyaluronidase, administered by subcutaneous (SC; under the skin) injection in combination with intravenous (IV) chemotherapy, for the treatment of early and metastatic HER2-positive breast cancer. Based on this recommendation, a final decision regarding the approval of Phesgo is expected from the European Commission in the near future.

“Our commitment to transforming the lives of people with breast cancer goes beyond improving efficacy outcomes,” said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. “Today's recommendation is another important step forward in redefining the standard of care for people with HER2-positive breast cancer in Europe by potentially offering a faster and less invasive way to receive treatment with Perjeta and Herceptin.”

SC administration of Phesgo takes approximately eight minutes for the initial loading dose and approximately five minutes for each subsequent maintenance dose.¹ This is compared to approximately 150 minutes for infusion of a loading dose of Perjeta and Herceptin using the standard IV formulations, and between 60-150 minutes for subsequent maintenance infusions of the two medicines.^{2,3}

The recommendation from the CHMP is based on results from the pivotal phase III FeDeriCa study, which showed that treatment with Phesgo produced non-inferior levels of Perjeta and Herceptin in the blood when compared to IV administration of the two medicines. The safety profile of Phesgo with chemotherapy was comparable to IV administration of Perjeta plus Herceptin and chemotherapy, and no new safety signals were identified, including no meaningful difference in cardiac toxicity. The most common adverse events in both arms were alopecia, nausea, diarrhoea and anaemia.^{1,7}

The U.S. Food and Drug Administration recently expedited the approval of Phesgo for the treatment of early and metastatic HER2-positive breast cancer. Based on the decision of the treating physician and the preference of the patient, it can be administered by a healthcare professional in a treatment centre or in a patient's home.

The Herceptin SC vial is approved for the treatment of HER2-positive breast cancer in more than 100 countries worldwide and provides a convenient treatment option for patients and cost-savings for healthcare systems.^{5,6} Phesgo is another step forward in highlighting Roche's commitment to improving patients' experience of cancer treatment, looking beyond efficacy outcomes and focusing on more flexible treatment solutions.

About the FeDeriCa study

FeDeriCa is an international, multi-centre, two-arm, randomised, open-label, pivotal phase III study evaluating the pharmacokinetics, efficacy and safety of subcutaneous injection of Phesgo in combination with chemotherapy, compared with standard intravenous (IV) infusions of Perjeta and Herceptin in combination with chemotherapy, in 500 people with HER2-positive early breast cancer 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}), when compared to IV administration of Perjeta. Secondary endpoints include safety; minimum levels of Herceptin in the blood during a given dosing interval (C_{trough}); and total pathological complete response, meaning there is no tumour tissue detectable in the tissue removed at the time of surgery.

Data from the FeDeriCa study were presented at the San Antonio Breast Cancer Symposium in December 2019. The FeDeriCa study met its primary endpoint of non-inferior levels of Perjeta in the blood. The geometric mean ratio (GMR; a type of average used when assessing pharmacokinetics) for the primary endpoint was 1.22 (90% CI: 1.14 to 1.31), with the lower limit of the 90% CI of the GMR=1.14 \geq 0.80 (the pre-specified non-inferiority margin). A secondary endpoint of non-inferior levels of Herceptin was also met, with blood concentrations for people receiving Phesgo non-inferior to those receiving IV Herceptin (GMR=1.33 [90% CI: 1.24 to 1.43]; lower limit of 90% CI of GMR=1.24 \geq 0.80). A non-inferiority endpoint was chosen for the study to ensure that people were receiving sufficient dosing with Perjeta and Herceptin as compared to the established IV doses at the same treatment intervals.^{7,8}

About Phesgo

Phesgo is a new fixed-dose subcutaneous (SC) formulation that combines the same monoclonal antibodies as Perjeta and Herceptin with Halozyme Therapeutics' Enhanze[®] drug delivery technology.^{1,9} This is the first time that Roche has combined two monoclonal antibodies that can be administered by a single SC injection.

Halozyme's Enhance drug delivery technology may enable and optimise SC drug delivery for appropriate co-administered therapeutics. The technology is based on a proprietary recombinant human hyaluronidase PH20 (rHuPH20), an enzyme that temporarily degrades hyaluronan – a glycosaminoglycan or chain of natural sugars in the body – to aid in the dispersion and absorption of other injected therapeutic drugs.⁹

Pertuzumab in Phesgo is the same monoclonal antibody as in intravenous (IV) Perjeta, and trastuzumab in Phesgo is the same monoclonal antibody as in IV 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. The combination of Perjeta and Herceptin is thought to provide a more comprehensive, dual blockade of the HER signalling pathways.^{10,11}

Phesgo is approved in the US for the treatment of early and metastatic HER2-positive breast cancer. The approved indications for Phesgo mirror those of Perjeta.

The standard IV formulation of Perjeta in combination with IV Herceptin and chemotherapy (the Perjeta-based regimen) is approved in over 100 countries for the treatment of both early and metastatic HER2-positive breast cancer. In the neoadjuvant (before surgery) early breast cancer (eBC) setting, the Perjeta-based regimen has been shown to almost double the rate of pathological complete response compared to Herceptin and chemotherapy.¹² Additionally, the combination has been shown to significantly reduce the risk of recurrence of invasive disease or death in the adjuvant (after surgery) eBC setting.¹³ In the metastatic setting, the combination has shown an unprecedented survival benefit in previously untreated (first-line) patients with HER2-positive metastatic breast cancer.¹⁴

About Roche's medicines for HER2-positive breast cancer

Roche has been leading research into the HER2 pathway for over 30 years and is committed to improving the health, quality of life and survival of people with both early and metastatic HER2-positive disease. HER2-positive breast cancer is a particularly aggressive form of the disease that affects approximately 25-30% of patients.¹⁵ Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin, Perjeta and Kadcyła® (trastuzumab emtansine). Eligibility for treatment with Roche's HER2-targeted medicines is determined via a diagnostic test which identifies people who will likely benefit from these medicines at the onset of their disease.

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader

in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the eleventh consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

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