

## **FDA approves Roche's Phesgo (fixed-dose combination of Perjeta and Herceptin for subcutaneous injection) for HER2-positive breast cancer**

- **Phesgo offers faster administration of Perjeta and Herceptin under the skin in just minutes, compared to hours with standard intravenous administration**
- **Data showed that 85% of patients preferred Phesgo compared to standard intravenous administration**

Basel, 29 June 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has approved 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. This is the first time that Roche has combined two monoclonal antibodies that can be administered by a single SC injection.

“The FDA approval of Phesgo reflects our commitment to improving outcomes for the many people living with HER2-positive breast cancer,” said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. “Phesgo offers a treatment administration that supports the needs and preferences of individual patients, and helps to meet the increasing demand across the healthcare system for faster and more flexible treatment options.”

Phesgo is available in one single-dose vial. Administration can take approximately eight minutes for the initial loading dose and approximately five minutes for each subsequent maintenance dose. <sup>[1]</sup> This is compared to approximately 150 minutes for a sequential 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. <sup>[2, 3]</sup> Phesgo can be administered by a healthcare professional in a treatment centre or at a patient's home.

The approval is based on results from the pivotal phase III FeDeriCa study, which met its primary endpoint with Phesgo showing non-inferior levels of Perjeta in the blood during a given dosing interval (C<sub>trough</sub>), when compared to IV administration of Perjeta. 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. <sup>[1, 4]</sup>

The phase II PHranceSCa study showed that 85% (136/160) of people receiving treatment for HER2-positive breast cancer preferred treatment under the skin to IV administration due to less time in the clinic and more comfortable treatment administration. <sup>[1]</sup>

### **About the FeDeriCa study** <sup>[4, 5]</sup>

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 (Ctough), when compared to IV administration of Perjeta. Secondary endpoints include safety; minimum levels of Herceptin in the blood during a given dosing interval (Ctough); 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 the fixed-dose combination 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.

### **About the PHranceSCa study** <sup>[6]</sup>

PHranceSCa is a phase II, randomised, multi-centre, multinational, open-label, cross-over study evaluating patient preference for and satisfaction with subcutaneous administration of Phesgo in 160 people with HER2-positive early breast cancer. All patients completed neoadjuvant (before surgery) treatment with Perjeta, Herceptin and chemotherapy and had surgery before randomisation. The primary endpoint of the study is the percentage of participants who indicate that they prefer treatment with Phesgo compared to the standard intravenous (IV) formulations of Perjeta and Herceptin. Secondary endpoints include participant-reported satisfaction and health-related quality of life outcomes; healthcare professionals' perceptions of time and resource use and convenience compared with IV formulations; as well as the safety and efficacy of each study regimen.

Interim results from the PHranceSCa study were presented at the European Society for Medical Oncology Breast Cancer Virtual Meeting in May 2020. Primary results will be presented at a medical conference later in 2020.

### **About Phesgo**

Phesgo is a new fixed-dose subcutaneous (SC) formulation that combines Perjeta and Herceptin with Halozyme Therapeutics' Enhance<sup>®</sup> drug delivery technology. <sup>[1]</sup> 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. [7]

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. [8, 9]

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. [10] 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. [11] In the metastatic setting, the combination has shown an unprecedented survival benefit in previously untreated (first-line) patients with HER2-positive metastatic breast cancer. [12]

#### **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 15-20% of patients. [13] Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin, Perjeta and Kadcyla® (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](http://www.roche.com).

All trademarks used or mentioned in this release are protected by law.

## References

- [1] US Food and Drug Administration. Prescribing information for Phesgo.
- [2] US Food and Drug Administration. Prescribing Information for Herceptin. [Internet; cited June 2020]. Available from: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2010/103792s5250lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/103792s5250lbl.pdf).
- [3] US Food and Drug Administration. Prescribing Information for Perjeta [Internet; cited June 2020]. Available from: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2017/125409s113s118lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125409s113s118lbl.pdf).
- [4] Tan A, et al. Subcutaneous administration of the fixed-dose combination of trastuzumab and pertuzumab in combination with chemotherapy in HER2-positive early breast cancer: primary analysis of the phase III, multicenter, randomized, open-label, two-arm FeDeriCa study. Presented at SABCS, 2019 Dec 10-14; San Antonio, Texas. Abstract #PD4-07.
- [5] Clinical trials.gov. A Study to Evaluate the Pharmacokinetics, Efficacy, and Safety of Subcutaneous Administration of the Fixed-Dose Combination of Pertuzumab and Trastuzumab in Combination With Chemotherapy in Participants With HER2-Positive Early Breast Cancer (FeDeriCa). [Internet; cited June 2020]. Available from: <https://clinicaltrials.gov/ct2/show/NCT03493854>.
- [6] Clinical trials.gov. A Study to Evaluate Patient Preference and Satisfaction of Subcutaneous Administration of the Fixed-Dose Combination of Pertuzumab and Trastuzumab in Participants With HER2-Positive Early Breast Cancer (PHranceSCa). [Internet; cited June 2020]. Available from: <https://clinicaltrials.gov/ct2/show/NCT03674112>.
- [7] Halozyme. Enhance<sup>®</sup> Drug Delivery Technology. [Internet; cited June 2020]. Available from: <https://www.halozyme.com/enhance/overview/default.aspx>.
- [8] Iqbal N, Iqbal N. Human Epidermal Growth Factor Receptor 2 (HER2) in Cancers: Overexpression and Therapeutic Implications. *Mol Biol Int*. 2014;2014:852748.
- [9] Baselga J, Swain SM. Novel anticancer targets: revisiting ERBB2 and discovering ERBB3. *Nat Rev Cancer* 2009;9:463-75.
- [10] Gianni L, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. *Lancet Oncol*. 2012;13(1):25-32.
- [11] Minckwitz G, et al. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. *N Engl J Med*. 2017;13;377(2):122-31.
- [12] Swain SM, et al. Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. *N Engl J Med*. 2015;19;372(8):724-34.
- [13] Wolff AC, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. *J Clin Oncol*. 2013;31(31):3997-4013.

## Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: [media.relations@roche.com](mailto:media.relations@roche.com)

- Nicolas Dunant (Head)
- Patrick Barth
- Daniel Grotzky
- Karsten Kleine
- Nathalie Meetz
- Barbara von Schnurbein