Phesgo Dosing and Administration Recommendations

This article responds to your request for information on Phesgo® (pertuzumab, trastuzumab, and hyaluronidase) subcutaneous injection and dosing and administration recommendations.

Please refer to the locally approved dosing information provided in the Phesgo package insert or prescribing information. Any deviation from this information is considered off-label and any treatment decisions based on such deviations are the full responsibility of the prescribing physician.

In brief

- There are no recommendations for administering premedications in the Phesgo prescribing information.
- The recommended loading dose of Phesgo is 1200 mg pertuzumab/600 mg trastuzumab administered, followed every 3 weeks thereafter by a maintenance dose of 600 mg pertuzumab/600 mg trastuzumab.
    - If a patient experiences a delayed or missed dose, they may need to be administered the loading dose of Phesgo again.
- Phesgo is a fixed dose combination of pertuzumab and trastuzumab and is dosed irrespective of patient body weight, with no upper or lower weight limit.
    - Rates of total pathological complete response by body mass index was a pre-specified exploratory analysis in the FeDeriCa study. No association was observed between body weight and total pathological complete response
    - A descriptive analysis of adverse events by body weight quartile was performed at the updated safety analysis of FeDeriCa. Adverse event incidence rates were balanced across body weight quartiles and between treatment arms, including the lower quartile.
- Patients should be observed during Phesgo administration and for 30 minutes following the administration of a loading dose, or 15 minutes following a maintenance dose.

Administering premedication

There are no recommendations for administering premedications in the Phesgo prescribing information.[1]

Premedication protocol in the Phase 3 FeDeriCa study

In the pivotal FeDeriCa study, while not required, standard premedications for neoadjuvant chemotherapy could be administered in line with local practice. This included, but was not limited to, analgesics, corticosteroids, and antiemetics.

Loading and maintenance dose

The recommended loading dose of Phesgo is 1200 mg pertuzumab/600 mg trastuzumab administered over approximately 8 minutes.[1] This is followed every 3 weeks thereafter by a maintenance dose of 600 mg pertuzumab/600 mg trastuzumab administered over approximately 5 minutes. Both loading and maintenance dose is irrespective of patient body weight.[1]

Reloading following delayed or missed doses

If a patient experiences a delayed or missed dose, the next dose should be administered as soon as possible.[1] Do not wait until the next planned dose.

Depending on the time between two sequential doses, the patient may need to be administered the loading dose again.[1] Refer to Table 1 for recommendations on re-loading Phesgo.

Table 1. Recommendations regarding delayed or missed doses

If the time between two sequential doses is...	Then administer a...
Less than 6 weeks	Maintenance dose - Administer 600 mg pertuzumab/600 mg trastuzumab over approximately 5 minutes.
6 weeks or longer	Loading dose - re-administer the 1200 mg pertuzumab/600 mg trastuzumab over approximately 8 minutes.

Once the patient has received either a loading or maintenance dose following the delay, the 3 weekly interval should be based on the latest dose, rather than the prior schedule.[1]

Switching from IV Perjeta and IV Herceptin

In patients already receiving IV Perjeta and IV Herceptin, the initial dose of Phesgo should be the maintenance dose of 600 mg pertuzumab/600 mg trastuzumab, provided it has been less than 6 weeks since their last dose.[1] If it has been equal to or more than 6 weeks, then the loading dose of 1200 mg pertuzumab/600 mg trastuzumab should be given.

Dosing in underweight or overweight patients

Phesgo is a fixed dose combination of pertuzumab and trastuzumab and is dosed irrespective of patient body weight, with no upper or lower weight limit.[1]

BMI exploratory analysis from the Phase 3 FeDeriCa study

The Phase 3 FeDeriCa study assessed the pharmacokinetics, efficacy and safety of Phesgo compared to IV Perjeta and IV Herceptin.[2] Phesgo was administered in line with the approved dosing schedule, 1,200 mg pertuzumab/600 trastuzumab loading dose, followed by 600 mg pertuzumab/600 mg trastuzumab maintenance dose. Rates of total pathological complete response by body mass index was a pre-specified exploratory analysis in the study. As presented in Table 2, no association was observed between body weight and total pathological complete response.[3]

Table 2. Rates of tpCR by body mass index (ITT population)[3]

Body mass index (WHO classification), n/N (%; 95% CI)	Perjeta IV + Herceptin IV (n = 252)	Phesgo (n = 248)
Underweight (<18.5 kg/m2)	3/3 (100; 29.24-100)	3/7 (42.9; 9.9-81.59)
Normal (18.5 to <25 kg/m2)	71/120 (59.2; 49.82-68.05)	70/112 (62.5; 52.85-71.47)

Overweight (25 to <30 kg/m2)	45/80 (56.3; 44.7-67.32)	49/75 (65.3; 53.46-75.96)
Obese (≥30 kg/m2)	31/49 (63.3; 48.29-76.58)	26/54 (48.1; 34.34-62.16)
Abbreviations: CI=confidence interval; ITT=intent-to-treat; tpCR=total pathological complete response; WHO=world health organization.		

Safety assessment from the Phase 3 FeDeriCa study

A safety evaluation of the FeDeriCa study performed a descriptive analysis of adverse events by body weight quartile.[4] Shown in Table 3, adverse event incidence rates were balanced across body weight quartiles and between treatment arms, including the lower quartile.

Table 3. Summary of AEs by body weight quartile (safety population)[4]

	Perjeta IV + Herceptin IV (n = 252)	Phesgo (n = 248)
Treatment-emergent serious AE*, n (%)	50 (19.8)	47 (19)
Q1: <58 kg Q2: 58-65 kg Q3: 65-77 kg Q4: >77 kg	10 (4) 9 (3.6) 16 (6.3) 15 (6)	12 (4.8) 9 (3.6) 8 (3.2) 18 (7.3)
Cardiac dysfunction†, n(%)	66 (26.2)	53 (21.4)
Q1: <58 kg Q2: 58-65 kg Q3: 65-77 kg Q4: >77 kg	19 (7.5) 11 (4.4) 22 (8.7) 14 (5.6)	15 (6) 9 (3.6) 8 (3.2) 21 (8.5)
LVEF decline‡, n (%)	17 (6.7)	13 (5.2)
Q1: <58 kg Q2: 58-65 kg Q3: 65-77 kg Q4: >77 kg	6 (2.4) 3 (1.2) 6 (2.4) 2 (0.8)	3 (1.2) 1 (0.4) 2 (0.8) 7 (2.8)
AE leading to withdrawal of HER2-targeted therapy, n (%)	15 (6)	12 (4.8)
Q1: <58 kg Q2: 58-65 kg Q3: 65-77 kg Q4: >77 kg	3 (1.2) 4 (1.6) 6 (2.4) 2 (0.8)	2 (0.8) 3 (1.2) 3 (1.2) 4 (1.6)
Notes: Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient. *Occurring on the day or after the first administration of study drug until 28 days after last study drug administration. †Cardiac failure (wide Standardized MedDRA queries). ‡LVEF decline of ≥10% points from baseline and to <50%. Abbreviations: AE=adverse event; H=trastuzumab; LVEF=left ventricular ejection fraction; P=pertuzumab; Q=quartile.		

Recommended observation times

It is recommended to closely observe a patient during and for a period of time after administration:[1]

- Initial loading dose — 30 minutes
- Subsequent maintenance dose —15 minutes.

Observation times from Phesgo clinical trials

A 30-minute initial observation time and a 15-minute maintenance observation time were recommended for the pivotal Phesgo clinical trials based on experience with other monoclonal antibodies, including Herceptin SC.[5] The Phase 3 FeDeriCa study evaluated the pharmacokinetics, efficacy and safety of Phesgo every 3 weeks compared to IV Perjeta and IV Herceptin in early breast cancer.[2] In the study, most infusion-related reactions and local injection reactions occurred during or immediately after HER2 treatment.[5] This resulted in the inclusion of these observation times in the Phesgo prescribing information.[2,5]

References

1. Roche Internal Regulatory Report. Accessed 21 June 2023.

2. Tan A, Im S, Mattar 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 the San Antonio Breast Cancer Symposium in San Antonio, TX; December 10-14, 2019. SABCS Poster #PD4-07.

3. Tan AR, Im S, Mattar A, et al. Fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injection plus chemotherapy in HER2-positive early breast cancer (FeDeriCa): a randomised, open-label, multicentre, non-inferiority, phase 3 study. [supplementary appendix appears online]. Lancet Oncol 2021;22:85-97. https://pubmed.ncbi.nlm.nih.gov/33357420

4. Im S, Tan AR, Mattar A, et al. Fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injection (PH FDC SC) plus chemotherapy in HER2-positive earlybreast cancer (EBC): Safety results from the adjuvant phase of the randomised, open-label, multicentre phase 3 (neo)adjuvant FeDeriCa study. Presented at the European Society for Medical Oncology Breast Cancer 2021 Virtual Congress May 5-8, 2021. ESMO Poster #476.

5. Roche Internal Clinical Report (FeDeriCa). Accessed 05 July 2023 .