Phesgo™ (pertuzumab/trastuzumab/hyaluronidase-zzxf) – New drug approval

- On June 29, 2020, the FDA announced the approval of Genentech's Phesgo (pertuzumab/trastuzumab/hyaluronidase-zzxf), for use:
    - In combination with chemotherapy for: (1) the neoadjuvant treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer; (2) the adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence.
    - In combination with docetaxel for the treatment of adult patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

- Patients should be selected for therapy based on an FDA-approved companion diagnostic test.

- Phesgo is administered as a subcutaneous (SC) injection. Trastuzumab in Phesgo is the same monoclonal antibody as in intravenous (IV) Herceptin® and pertuzumab in Phesgo is the same monoclonal antibody as in IV Perjeta®. The mechanisms of action of Perjeta and Herceptin are believed to complement each other, as both bind to the HER2 receptor, but to different places.

- The use of Phesgo in the neoadjuvant and adjuvant treatment setting was supported by evidence from adequate and well-controlled studies conducted with IV pertuzumab and IV trastuzumab administered in combination with chemotherapy in adults with HER2-overexpressing early breast cancer and additional pharmacokinetic and safety data that demonstrated comparable pharmacokinetics and safety profiles between Phesgo and IV pertuzumab and IV trastuzumab in FeDeriCa.

- FeDeriCa was an open-label, randomized study in 500 patients with operable or locally advanced HER2- positive breast cancer. Patients were randomized to receive 8 cycles of neoadjuvant chemotherapy with concurrent administration of 4 cycles of either Phesgo or IV pertuzumab and trastuzumab during cycles 5 to 8, followed by surgery. Following surgery, patients continued therapy with Phesgo or IV pertuzumab and trastuzumab as treated prior to surgery, for an additional 14 cycles, to complete 18 cycles of therapy.
    - Phesgo demonstrated non-inferiority for cycle 7 (ie, pre-dose cycle 8) pertuzumab serum C_{trough} (primary endpoint) vs. IV administered Perjeta.

- The use of Phesgo for metastatic breast cancer was supported by evidence from adequate and well-controlled studies conducted with IV pertuzumab and IV trastuzumab administered in combination with chemotherapy in adults with HER2-overexpressing metastatic breast cancer and additional pharmacokinetic and safety data that demonstrated comparable pharmacokinetics and safety profiles between Phesgo and IV pertuzumab and IV trastuzumab in FeDeriCa.

- Phesgo carries a boxed warning for cardiomyopathy, embryo-fetal Toxicity, and pulmonary toxicity.

- Additional warnings and precautions for Phesgo include exacerbation of chemotherapy-induced neutropenia and hypersensitivity and administration-related reactions.

- In neoadjuvant and adjuvant treatment of breast cancer, the most common adverse reactions (> 30%) with Phesgo use were alopecia, nausea, diarrhea, anemia, and asthenia.

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- In metastatic breast cancer (based on IV pertuzumab), the most common adverse reactions (> 30%) with pertuzumab in combination with trastuzumab and docetaxel were diarrhea, alopecia, neutropenia, nausea, fatigue, rash, and peripheral neuropathy.

- The recommended initial dose of Phesgo is 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase administered SC over approximately 8 minutes, followed every 3 weeks by a dose of 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase administered SC over approximately 5 minutes.

    - In the neoadjuvant treatment setting, Phesgo should be administered for 3 to 6 cycles as part of a treatment regimen for early breast cancer. Following surgery, patients should continue to receive Phesgo to complete 1 year of treatment (up to 18 cycles) or until disease recurrence or unmanageable toxicity, whichever occurs first, as a part of a complete regimen for early breast cancer.
    - In the adjuvant treatment setting, Phesgo should be administered for a total of 1 year (up to 18 cycles) or until disease recurrence or unmanageable toxicity, whichever occurs first, as part of a complete regimen for early breast cancer, including standard anthracycline- and/or taxane-based chemotherapy. Phesgo should be started on day 1 of the first taxane-containing cycle.
    - In the metastatic setting, Phesgo should be administered until disease progression or unmanageable toxicity, whichever occurs first.
    - Phesgo is for SC use only in the thigh. It should not be administered IV.
    - Phesgo should not be substituted for or with pertuzumab, trastuzumab, ado-trastuzumab emtansine (Kadcyla®), or fam-trastuzumab deruxtecan (Enhertu®).
    - Phesgo must always be administered by a healthcare professional.
    - Refer to the Phesgo drug label for additional dosing and administration recommendations.

- Genentech's launch plans for Phesgo are pending. Phesgo will be available as a solution in single-dose vials containing:

    - 1,200 mg pertuzumab, 600 mg trastuzumab, and 30,000 units hyaluronidase/15 mL (80 mg, 40 mg, and 2,000 units/mL)
    - 600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase/10 mL (60 mg, 60 mg, and 2,000 units/mL).