



Advancing Patient care in HER2+ Breast cancer: Patients assessment and Education Dual HER-2 blockade in SC administration

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Challenges: Subcutaneous drugs used in oncology

Patients assessment and Education

Dual HER-2 blockade in SC: (Phesgo)

PH FDC SC is the first formulation in oncology to combine two mAbs, Pertuzumab and Trastuzumab, in one vial for SC injection

NCCN Guideline 2024, Systemic adjuvant Treatment in Breast cancer



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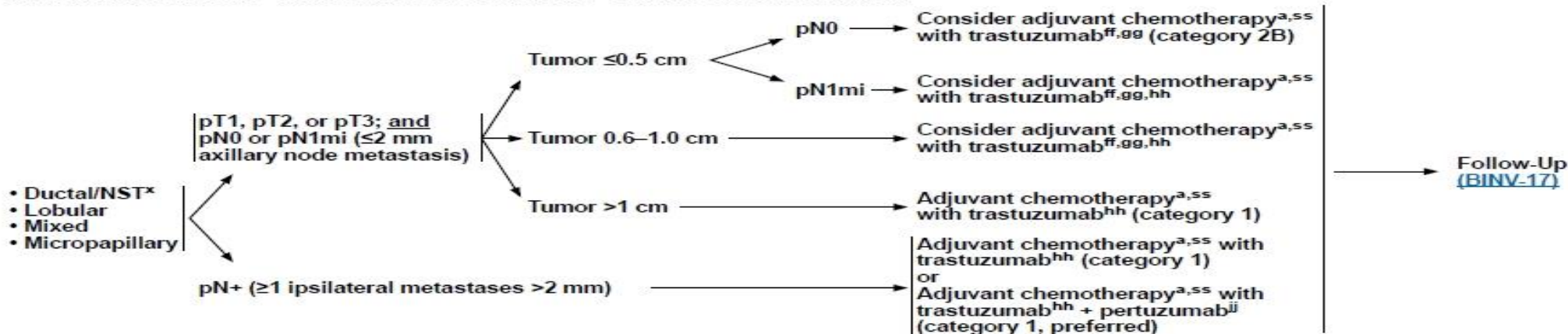


National
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NCCN Guidelines Version 1.2024 Invasive Breast Cancer

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SYSTEMIC ADJUVANT TREATMENT: HR-NEGATIVE – HER2-POSITIVE DISEASE^{d,t}



^a For tools to aid optimal assessment and management of older adults, see [NCCN Guidelines for Older Adult Oncology](#).

^d [Principles of Biomarker Testing \(BINV-A\)](#).

^t [Special Considerations for Breast Cancer in Males \(Sex Assigned at Birth\) \(BINV-J\)](#).

^x According to WHO, carcinoma of NST encompasses multiple patterns including medullary pattern, cancers with neuroendocrine expression, and other rare patterns.

^{ff} The prognosis of patients with T1a and T1b tumors that are pN0 is uncertain even when HER2 is amplified or overexpressed. This is a population of patients with breast cancer that was not studied in the available randomized trials. The decision for use of trastuzumab therapy in this cohort of patients must balance the known toxicities of trastuzumab, such as cardiac toxicity, and the uncertain, absolute benefits that may exist with trastuzumab therapy.

^{gg} Adjuvant chemotherapy with weekly paclitaxel and trastuzumab can be considered for pT1,N0,M0, HER2-positive cancers, particularly if the primary cancer is HR-negative. The absolute benefit of HER2-based systemic chemotherapy is likely negligible in patients with HR-positive cancers and tumor size bordering on T1mic (<1 mm), when the estimated recurrence risk is less than 5% and endocrine therapy remains a viable option for systemic treatment.

^{hh} Consider adjuvant bisphosphonate therapy for risk reduction of distant metastasis for 3–5 years in postmenopausal patients (natural or induced) with high-risk node-negative or node-positive tumors.

^{jj} Updated results from the adjuvant APHINITY trial in HER2-positive early breast cancer, with a median follow-up of 8.4 years, have confirmed the benefit of adding pertuzumab to trastuzumab plus chemotherapy in preventing recurrences.

^{ss} [Preoperative/Adjuvant Therapy Regimens \(BINV-L\)](#).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

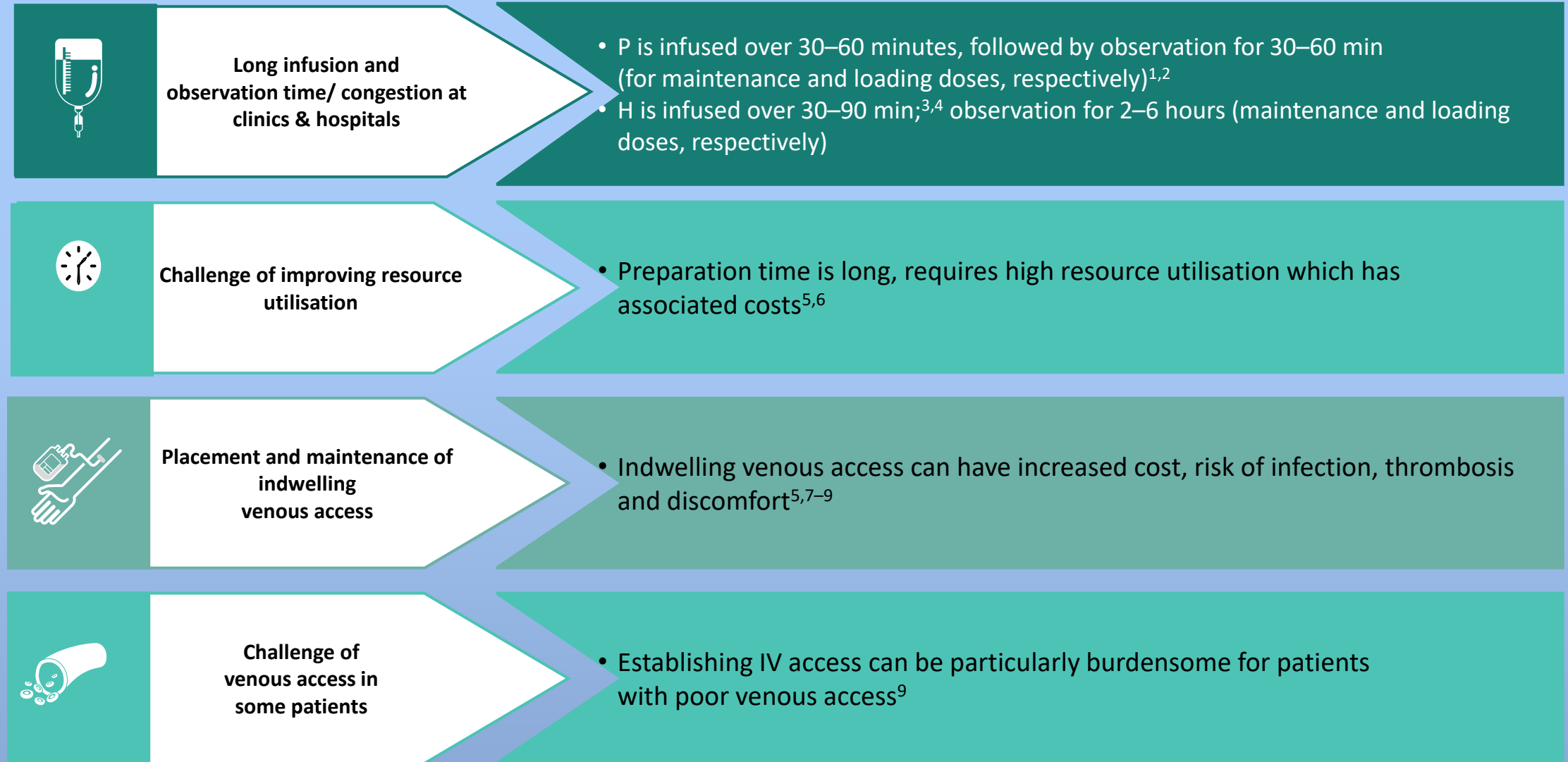
Subcutaneous drugs used in oncology



APPROVAL DATE	DRUG	USE
1969	Cytarabine	Treatment
1973	Bleomycin	Treatment
1989	Epoetin (Procrit®)	Supportive
1989	Goserelin acetate implant (Zoladex®) ^a	Treatment
1991	Filgrastim (Neupogen®)	Supportive
1991	Sargramostim (Leukine®)	Supportive
1992	Interleukin-2 (aldesleukin)	Treatment
1998	Octreotide (Sandostatin®)	Treatment
2001	Darbepoetin (Aranesp®)	Supportive
2002	Leuprolide acetate (Eligard®)	Treatment
2002	Pegfilgrastim (Neulasta®)	Supportive
2004	Azacitidine (Vidaza®)	Treatment

APPROVAL DATE	DRUG	USE
2007	Lanreotide (Somatuline® Depot)	Treatment
2008	Degarelix (Firmagon®)	Treatment
2010	Denosumab (Xgeva®)	Supportive
2012	Bortezomib (Velcade®)	Treatment
2012	Omacetaxine mepesuccinate (Synribo®)	Treatment
2017	Rituximab and hyaluronidase human (Rituxan Hycela®)	Treatment
2019	Trastuzumab and hyaluronidase-oysk (Herceptin Hylecta®)	Treatment
2020	Daratumumab and hyaluronidase-fihj (Darzalex Faspro™)	Treatment
2020 \	Pertuzumab, trastuzumab, and hyaluronidase-zzxf (Phesgo®)	Treatment

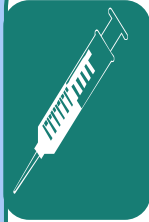
IV infusion of PERJETA–Herceptin is well established, but can present challenges to patients and healthcare systems





PH FDC SC is the first formulation in oncology to combine two mAbs, pertuzumab and trastuzumab, in one vial for SC injection

PH FDC SC



Contains the same antibodies as approved for IV PERJETA and Herceptin, but has a different route of administration^{1,2}



Is formulated with rHuPH20 (recombinant human hyaluronidase) to allow SC administration of higher drug volumes (15 mL loading dose; 10 mL maintenance dose)^{1,2}



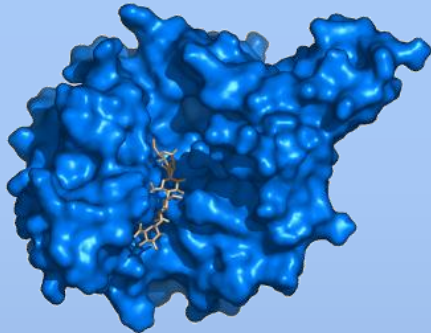
Is a ready-to-use fixed-dose formulation, administered by an SC injection in the thigh over 5–8 minutes²

Overview of recombinant human hyaluronidase



Formulation with the enzyme rHuPH20 offers potential for SC administration of large volumes of therapeutics

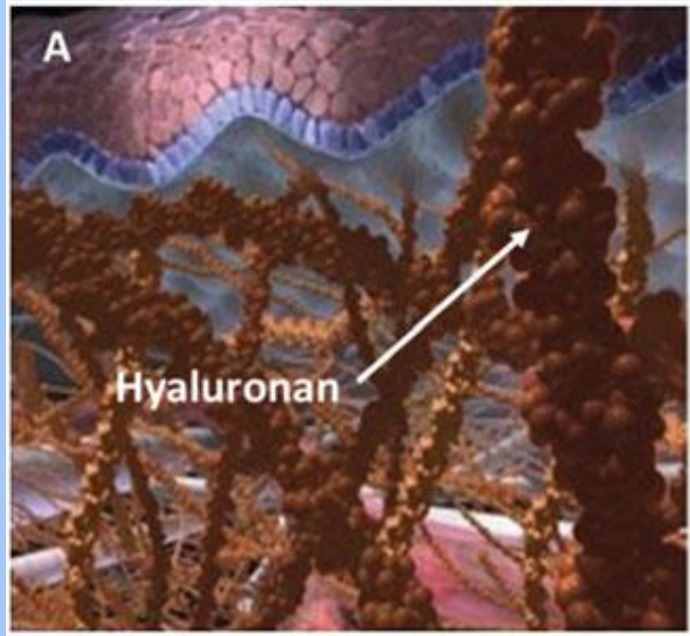
rHuPH20



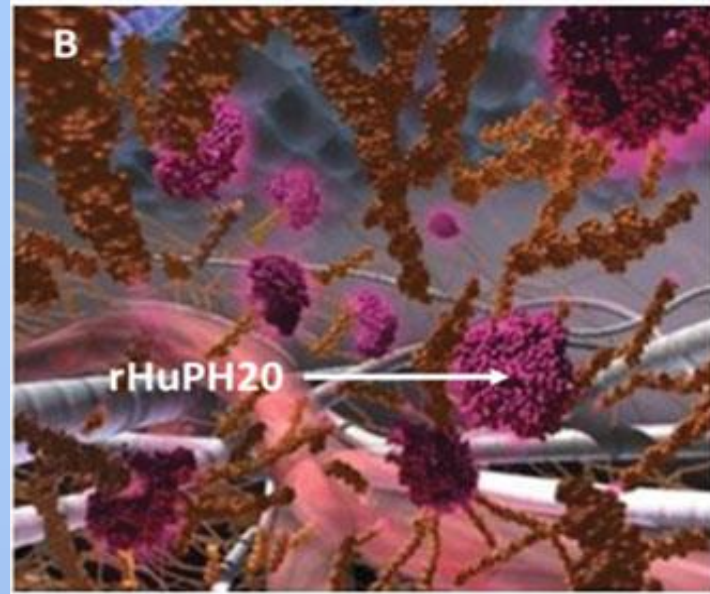
- Halozyme Therapeutics, Inc. has developed rHuPH20^{1,2}
- It is classified as a novel excipient
 - Enables the subcutaneous injection of large volumes of therapeutics^{2,3}
 - Has a short half-life^{2,3}
 - Has transient and reversible effects^{2,3}
- It is currently used in many SC formulations, including MabThera SC² and Herceptin SC,² and now in PH FDC SC⁴
- Positive opinion received through a centralised scientific advice procedure
 - Validated for use in every EU country and the US²



rHuPH20 mechanism of action

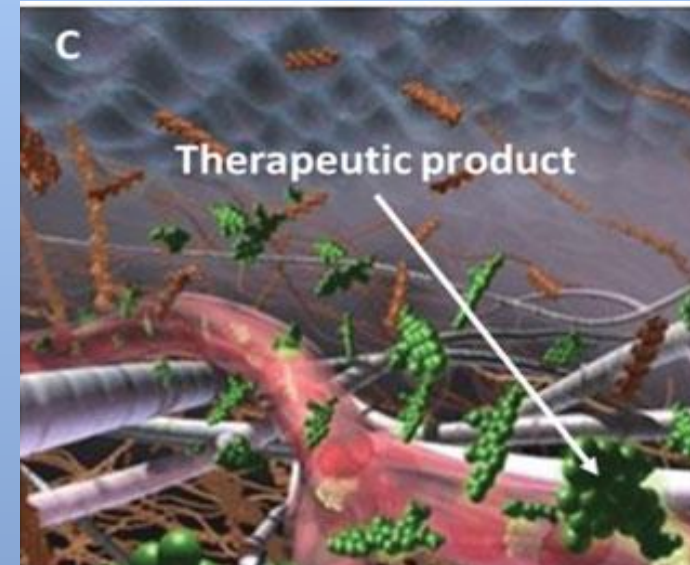


A: Hyaluronan creates a resistance to bulk fluid flow & limit large volume SC delivery, dispersion, and absorption



B: rHuPH20 depolymerizes hyaluronan

C: Facilitating SC bulk fluid flow And increasing the dispersion and absorption of therapeutic agent



rHuPH20 allows SC administration of volumes larger than 1 mL (rHuPH20: ช่วยให้บริหารยา SC ปริมาตรที่มีขนาดใหญ่กว่า 1 มล.มีประสิทธิภาพ)

Bolus injection of 10 mL 10% IgG solution

Without rHuPH20

Before infusion



Immediately post-infusion



With 2000 U/mL rHuPH20

Before infusion



Immediately post-infusion



Clinical Value: PH FDC SC could provide benefits in costs, time and reduction of patient/HCP burden



Shorter administration time (5–8 minutes) and observation period (15–30 minutes) of PH FDC SC may reduce the burden on patients, carers and providers^{1,2}



PH FDC SC has a less invasive administration (single SC injection) vs. IV (two separate IV infusions), freeing patients from the burden of IV-related pain, bruising and irritation³



Fixed-dose formulation may help reduce risk of dosing errors, reduce drug wastage and increase availability of pharmacy staff for other tasks^{2,4}



Reduced time required for drug preparation and administration with PH FDC SC vs. IV has the potential to relieve strain on infusion centres and allow greater patient access²



No new safety signals have been observed when switching from IV to PH FDC SC and vice versa⁵



What are the differences between PH FDC SC and Herceptin SC?

	Herceptin SC	PH FDC SC
Pharmaceutical form	Ready-to-use vial for manual injection ¹⁻³	
Delivery excipient	rHuPH20 (2000 U/mL) ^{1,2}	
Loading dose*	Fixed dose: 600 mg Herceptin SC (5 mL) ¹	Fixed dose: 1200 mg pertuzumab and 600 mg trastuzumab (15 mL) SC ^{2,3}
Administration time	Less than 5 minutes ¹	8 minutes
Observation time	6 hours	30 minutes
Maintenance dose*	Fixed dose: 600 mg Herceptin SC (5 mL) ¹	Fixed dose: 600 mg pertuzumab and 600 mg trastuzumab (10 mL) SC ^{2,3}
Administration time	Less than 5 minutes ¹	5 minutes
Observation time	2 hours	15 minutes
Key trials	HannaH, ⁴ PrefHer, ⁵ SafeHer, ⁶ MetaPHER ⁷	BO30185, ⁸ FeDeriCa, ³ PHranceSCa ⁹

* Administration/observation times vary according to local labels.
PH FDC SC, PERJETA–Herceptin fixed-dose combination for subcutaneous use;
rHuPH20, recombinant human hyaluronidase; q3w, every 3 weeks; SC, subcutaneous.

1. Herceptin SC SmPC 2019; 2. Roche, Data on file. WO40324 Protocol Version 2 – 2018; 3. Tan AR, *et al.* SABCS 2019 (Abstract PD4-07);
4. Ismael G, *et al.* *Lancet Oncol* 2012; **13**:869–878; 5. Pivot X, *et al.* *Ann Oncol* 2014; **25**:1979–1987; 6. Gligorov J, *et al.* *Eur J Cancer* 2017; **82**:237–246;
7. Kümmel S, *et al.* ESMO 2018 (Abstract 323P and poster presentation); 8. Kirschbrown WP, *et al.* *J Clin Pharmacol* 2019; **59**:702–716;
9. <https://clinicaltrials.gov/ct2/show/NCT03674112> (Accessed December 2019).



Assess management and nursing care: SC administration of large volumes: Pertuzumab+Trastuzumab

- เตรียมตัวผู้ป่วยและทวนสอบความถูกต้องของแผน/คำสั่งการรักษา
- **General patients information**
- **Monitoring Vital sign/ clinical signs**
- **Administration SC injection of large volumes**
- **Assess and evaluation sign and symptoms, clinical signs, AEs, Risk**
- **Administration related reactions**
- **Symptomatic LVD/ CHF: Congestive heart failure:**
- **Management and monitoring of Hypersensitivity and Anaphylaxis**
- ****ต้องมีระบบ Rapid response พร้อมใน setting**
- ****Monitor vital sign/ clinical signs ตลอดช่วงเวลาการบริหารยา**

General patients information



- **Safety profile is well known from Pertuzumab and Trastuzumab**
- **Phesgo SC administration has efficacy and safety perspective**
- **Most common Adverse Events: alopecia, diarrhea, asthenia, nausea, and anemia**
- **AEs specific to SC administration: local injection site reactions**
- **The majority of AEs reported were Grade 1 or 2 in severity**
- **Monitoring vital sign before and after administration.**
- **Sings and symptoms to notified staff**



Important Identified Risk



- **Administration related reactions:**
 - **local injection site reactions** reported 24 hours, with signs and symptoms such as erythema, induration, swelling, pain, hypoesthesia and discomfort.
 - **Injection related reaction**: A systemic reaction with symptoms such as chills, diarrhea, fatigue, headache, nausea, and pyrexia. Are likely due to a release of cytokines occurring within 24 hours of administration.
- **Hypersensitivity and Anaphylaxis Event: Systemic reaction, Signs and symptoms**
- **Management and monitoring of Hypersensitivity and Anaphylaxis**
- **Symptomatic LVD/ CHF: Congestive heart failure**
- **Asymptomatic Left ventricular dysfunction (LVD): Defined in LVEF of at least 10%-points from baseline and to <50%**
- **Management and monitoring of Oligohydramnios**

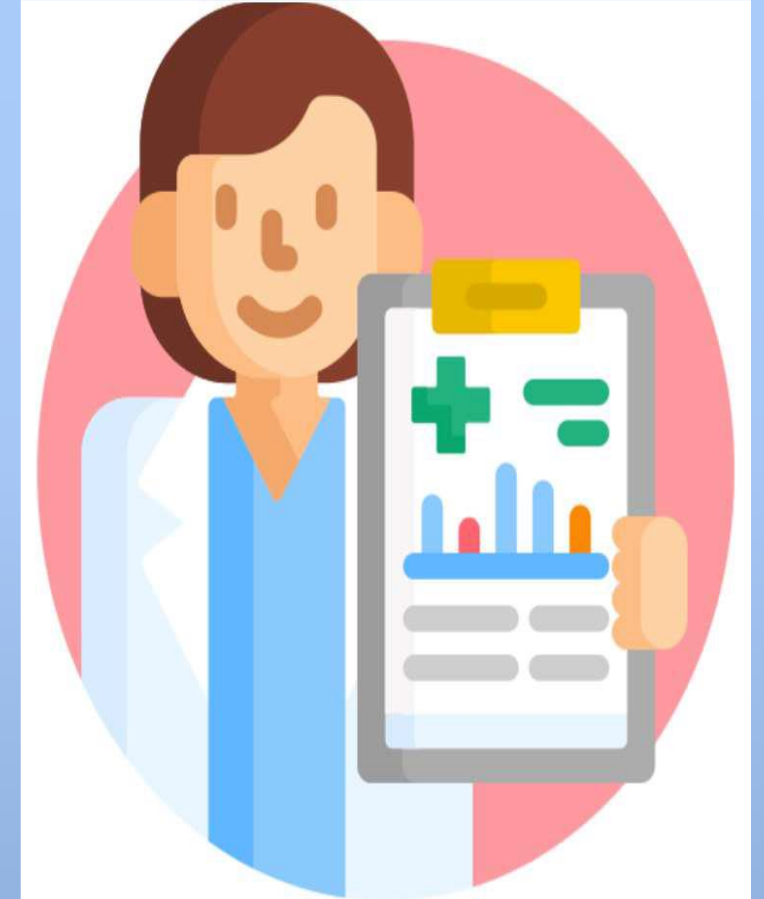


Safety management administration

- **ECG and a ECHO or MUGA assessment: LVEF Measurement of at least 50%**
- **Cardiac Monitoring:**
 - **LVEF**
 - Prior to 4th induction cycle; every 4th cycle thereafter
 - **ECG**
 - Prior to 1st Maintenance cycle; same timepoint as LVEF until Tx. discontinuation
- **Cardiac Monitoring:**
 - Cardiac Toxicity: Giredestrant and Bradycardia
 - Heart rate changes are dose related, stable and reversible
- **Monitoring vital sign and Rapid response system**

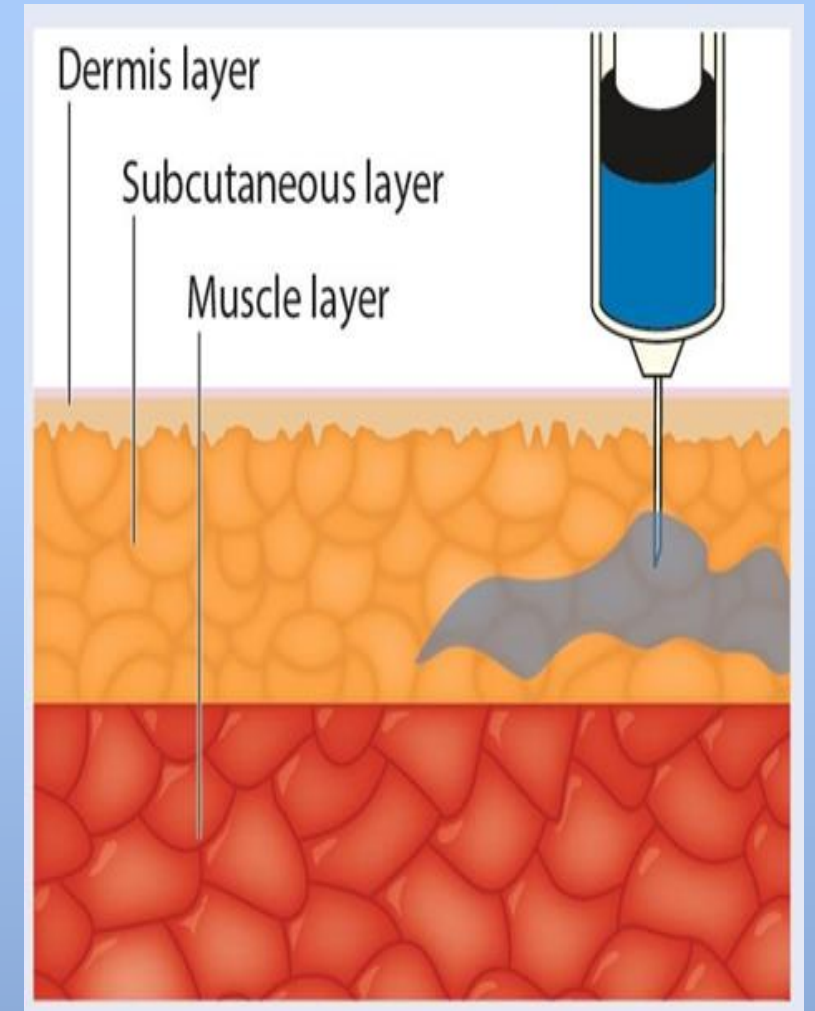
Patient education

- **Goals of therapy**
- **Basic understanding of chemotherapy/ immunotherapy mechanism of action**
- **Emphasis on patient-reported symptoms for prompt identification of toxicities**
- **Additional resources/tools**
- **Telephone, Line OA, E-mail, website**
- **Continuing care/ role of communication:**



Subcutaneous injection

- Require slow, sustained absorption of medication such as Insulin & Enoxaparin (less blood flow)
- Rotation site of injection when giving multiple doses
- Medication should be a small conc & volume is $< 1-2$ ml



SC injection: nursing intervention to reduce pain & drug leakage



INTERVENTION	REDUCED PAIN	REDUCED DRUG LEAKAGE
Inject slowly.	Yes	Yes
Orient needle bevel facing up.	Yes	No
Use smallest gauge needle appropriate for drug.	Yes	Yes
Use abdomen versus thigh when appropriate for drug.	Yes	No
Inject using 90-degree angle instead of 45-degree angle.	No	Yes
Wait at least 3 seconds before needle removal.	No	Yes
Use air lock technique.	Yes	Yes

Q: Abdomen VS thigh?

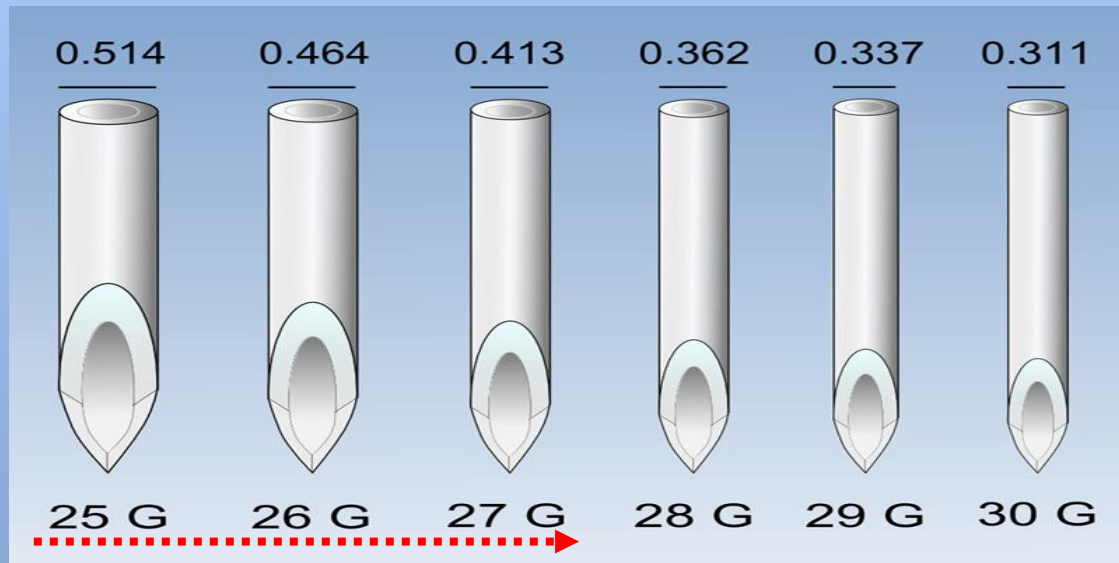


SC injection: Factors influence pain sensation

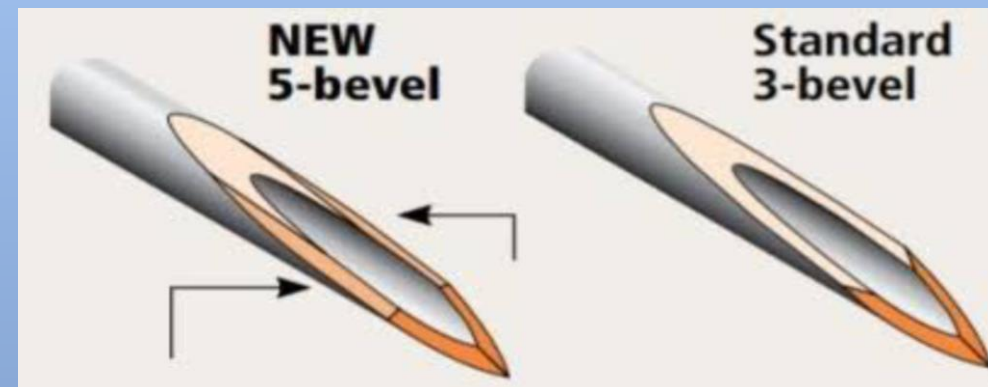
Needle : length, diameter, sharpness, bevel type , & lubricity

Average SC thickness based on anatomical location & gender

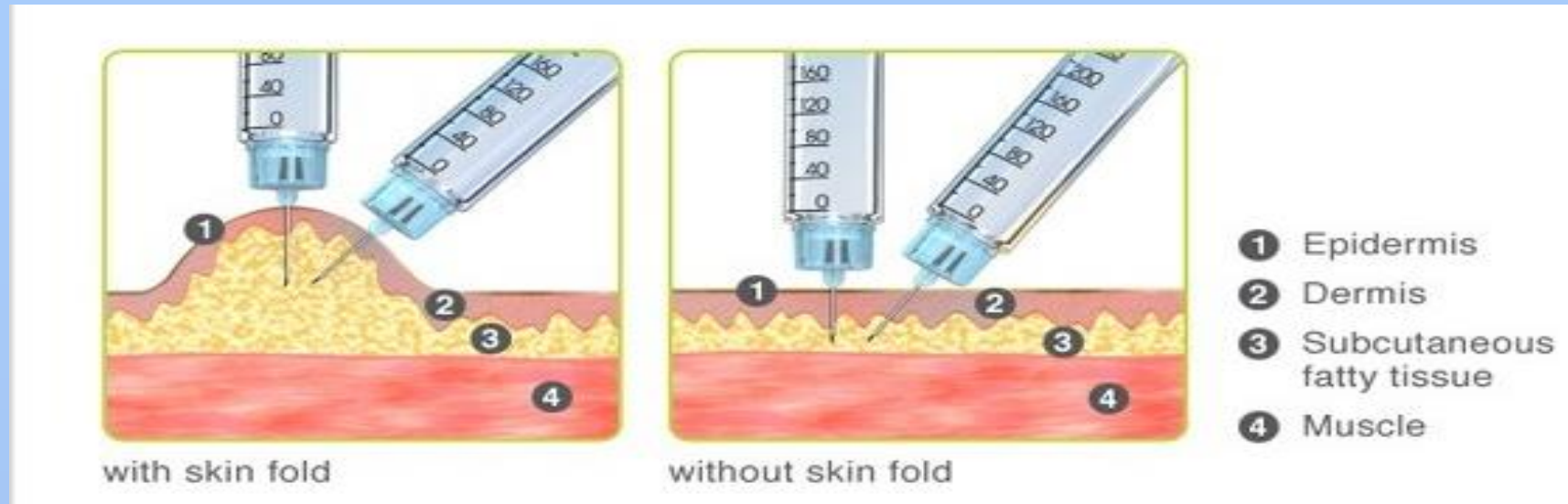
GENDER	ARM	THIGH	ABDOMEN
Female	13.7 mm	13.9 mm	15.9 mm
Male	8.4 mm	7.5 mm	12.9 mm



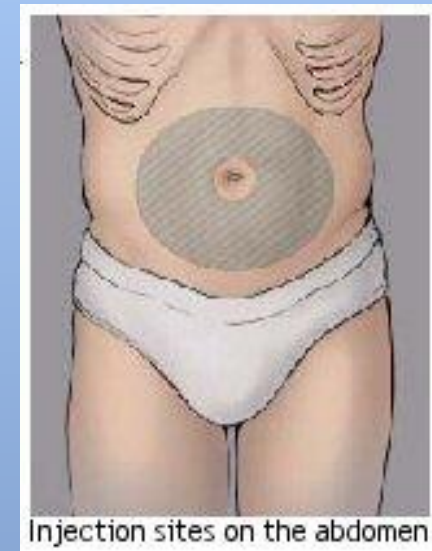
Pen: needle length 4-12.7 mm
Syringe: needle length 6-12.7 mm



SC Injection technique



SC Injection sites



Why dose phesgo inject into thigh?

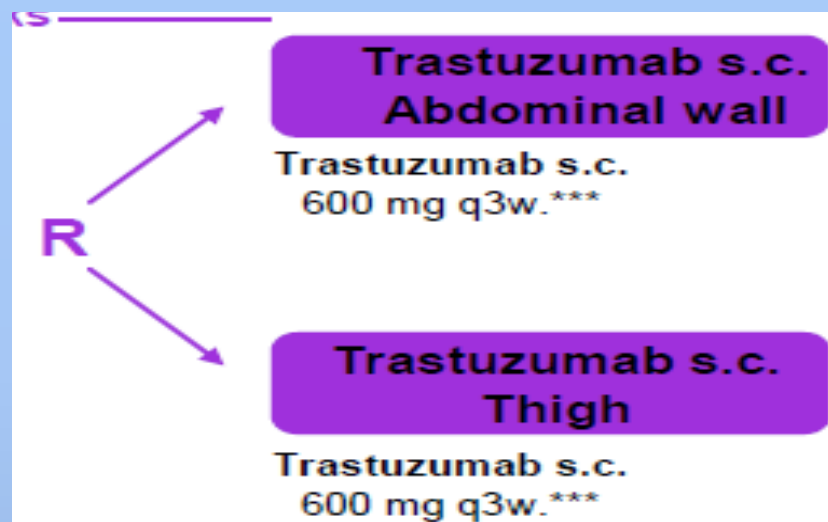
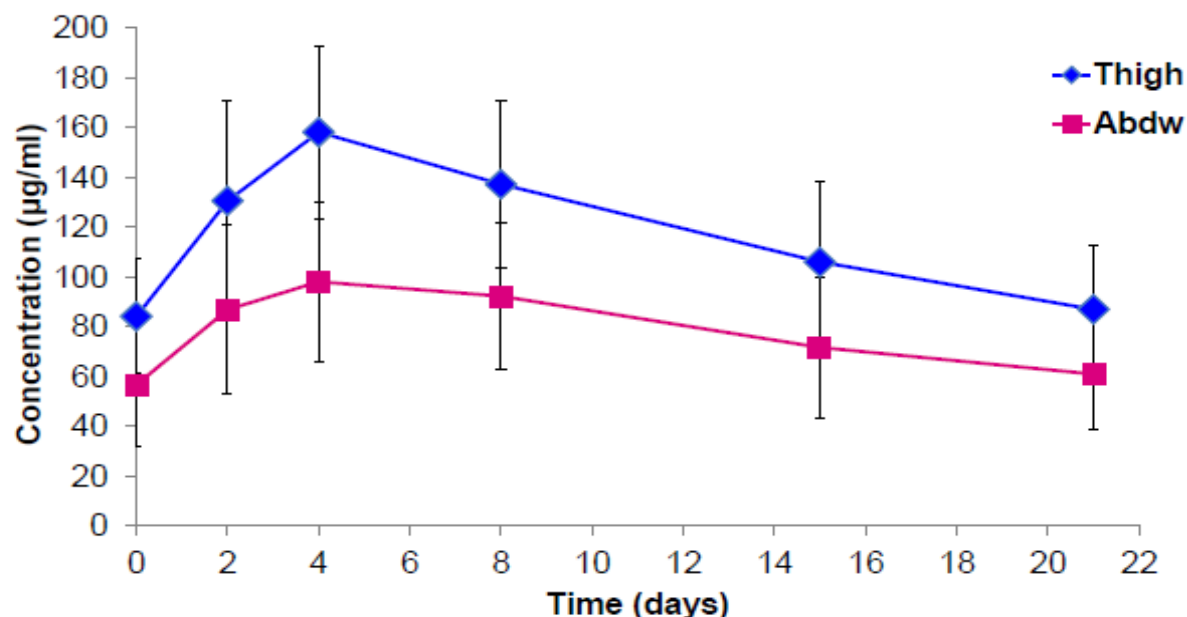


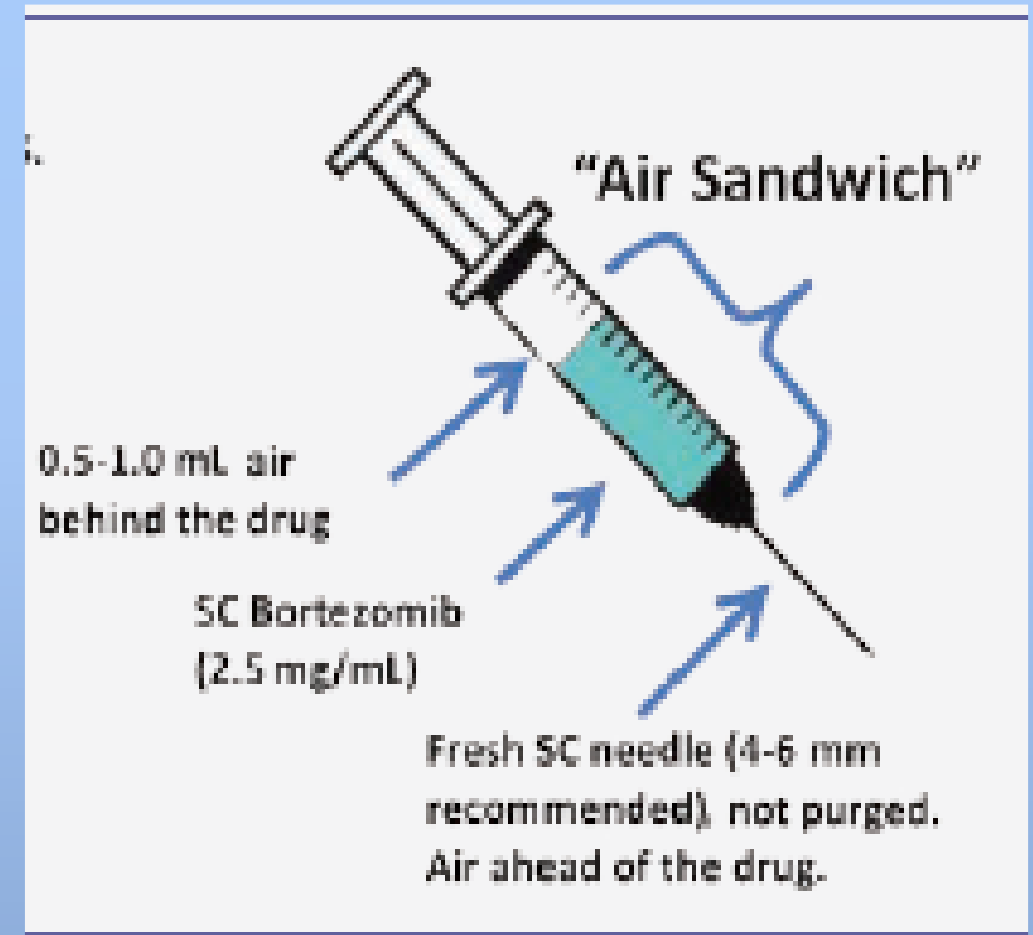
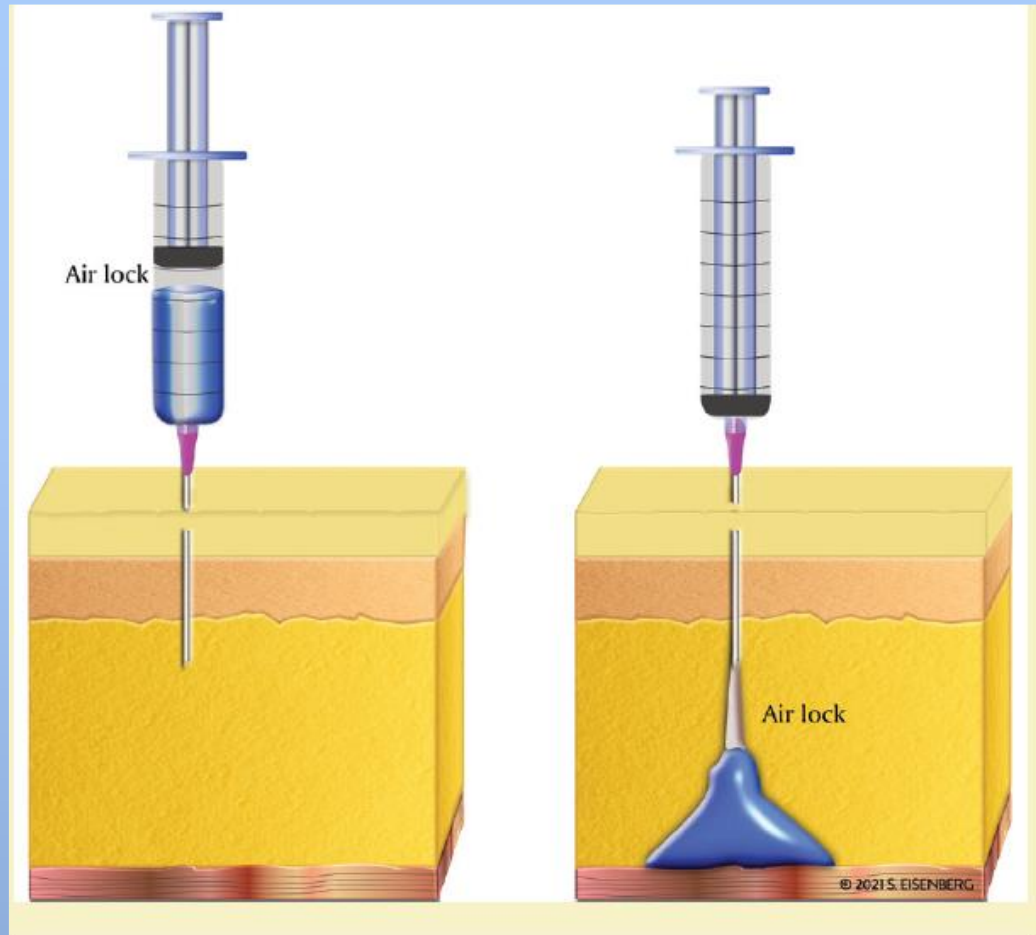
Figure 2. Mean plasma concentration-time profile of the s.c. trastuzumab



Conclusions

- Bioavailability of the s.c. trastuzumab as reflected by peak and total exposure measured in cycle 7 was approximately 30% higher if administered into the thigh than into the abdominal wall in pts with HER2-positive primary breast cancer treated with dose-dense CT plus i.v. trastuzumab.
- PK parameters of the s.c. trastuzumab administered into the thigh were in line with those from the HannnaH study¹.
- No increased toxicity was observed in both treatment groups.
- Study limitations were that no cross-over design was used and the number of patients satisfying criteria for pp-set were different in the groups.

SC administration by using AIR lock or AIR SANDWICH technique

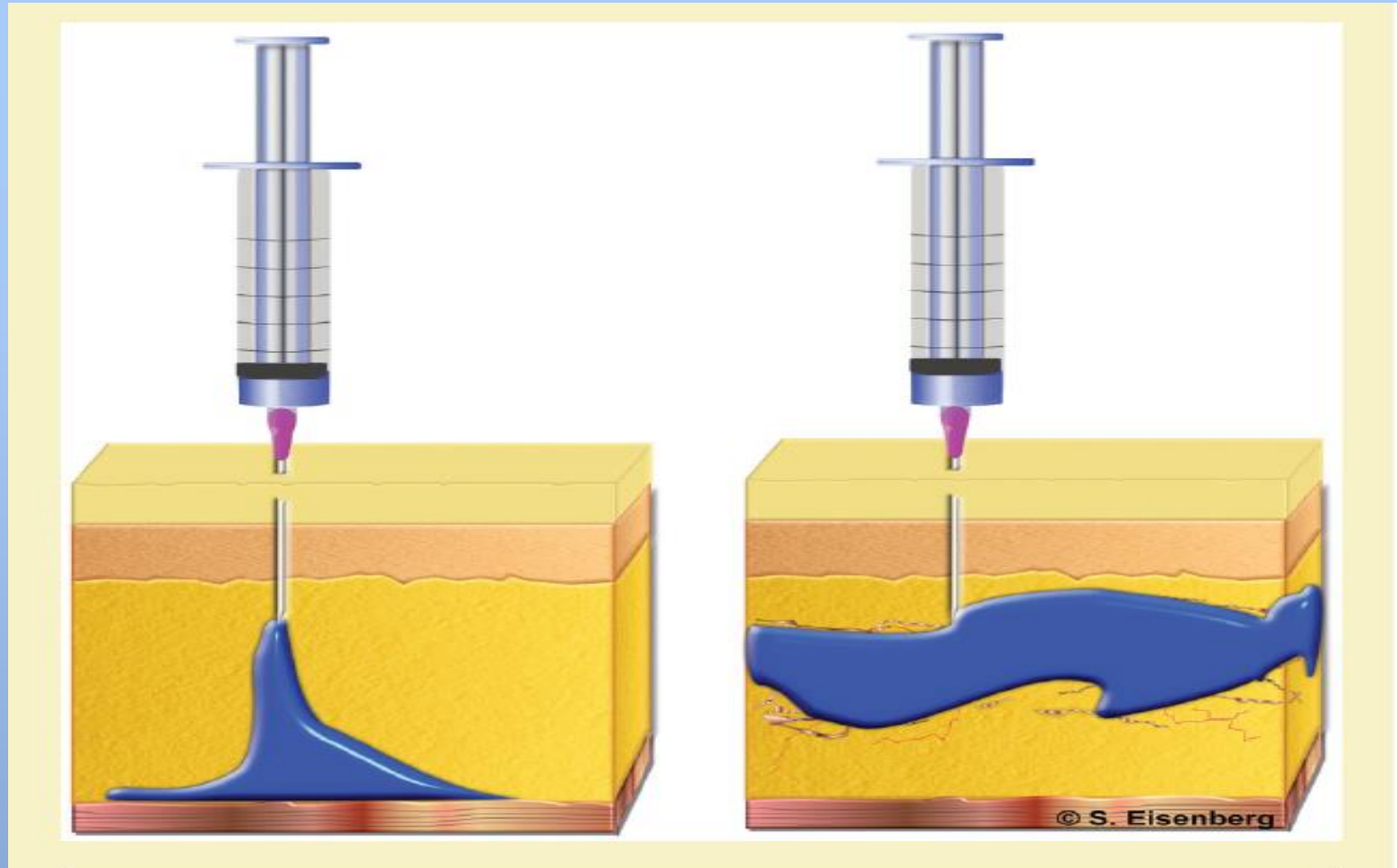


SC administration: distribution of medication based on injection rate

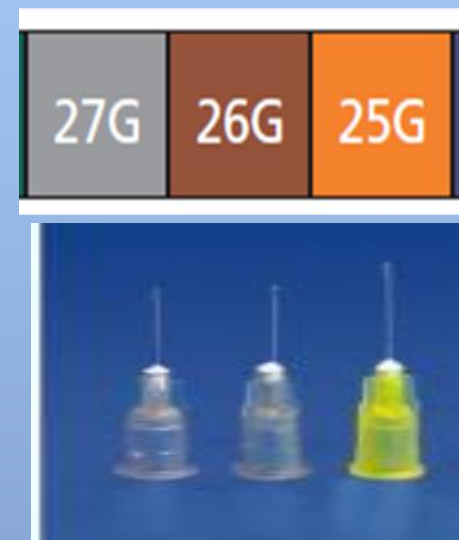
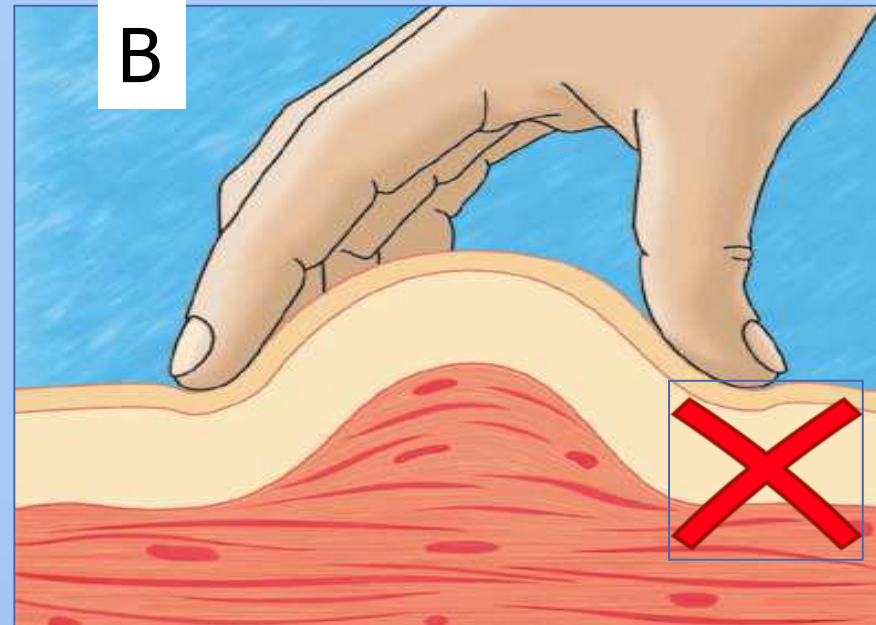
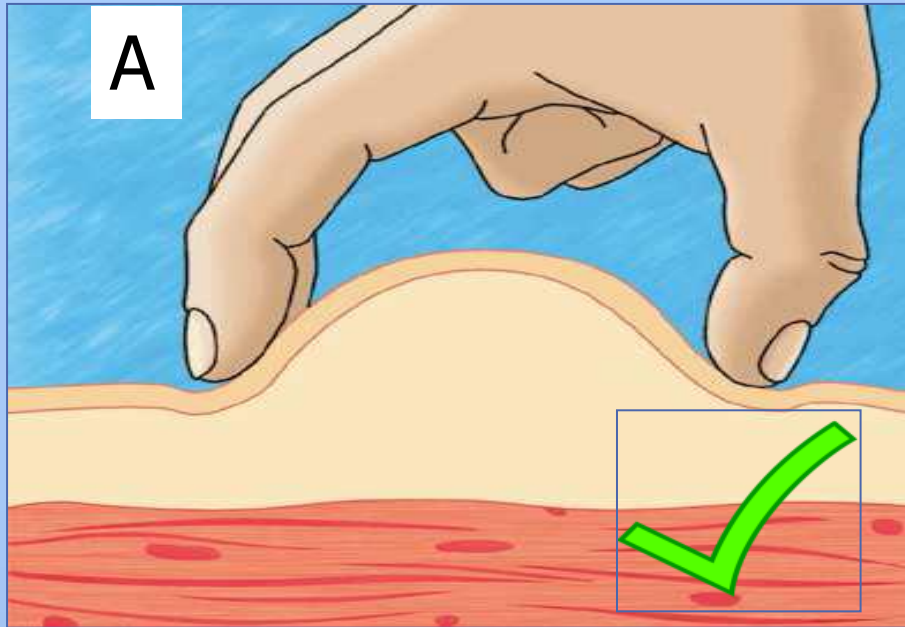
การบริหารยา SC: การกระจายตัวของยาตามอัตราการฉีด



Q : slow injection VS faster injection?



Pinch- up technique





SUBCUTANEOUS MONOCLONAL ANTIBODIES AND ADMINISTRATION RECOMMENDATIONS

DRUG	INJECTION TIME (MINUTES)	LOCATION	NEEDLE GAUGE
Darzalex Faspro[®]			
15 ml	3-5	Abdomen	23-25 (3/8"-1") at 45-degree angle
Herceptin Hylecta[®]			
5 ml	2-5	Thigh	25-27 (5/8")
Phesgo[®]			
15 ml loading	8	high	25-27 (3/8"-5/8")
10 ml maintenance	5	high	25-27 (3/8"-5/8")
Rituxan Hycela[®]			
11.7 ml (non-Hodgkin lymphoma)	5	Abdomen	25-27
13.4 ml (chronic lymphocytic leukemia)	7	Abdomen	25-27

P:T = 1200:600

P:T = 600:600



Pertuzumab/Trastuzumab (phesgo) SC administration

- **Wash your hands with water or alcohol hand rub**
- **Let the patient in the procedure room**
- **Required comfortable position ; supine/sitting position**
- **Record vital signs ; temperature, BP , PR & RR**
 - **Administration time Observation time (15-30 min): record vital signs ; temperature, BP , PR & RR and clinical signs**





Pertuzumab/Trastuzumab (phesgo) SC administration

- **Select & assess an injection site @ both thighs: previous site administration, sign of infection/inflammation, area of RT?**

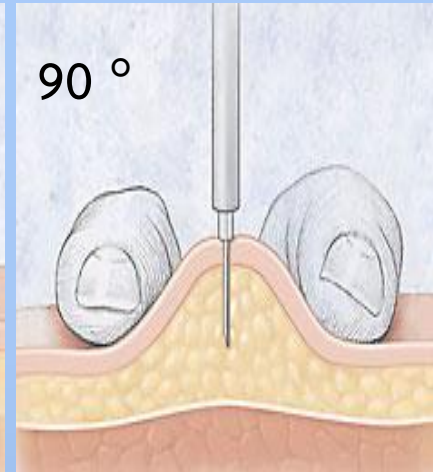
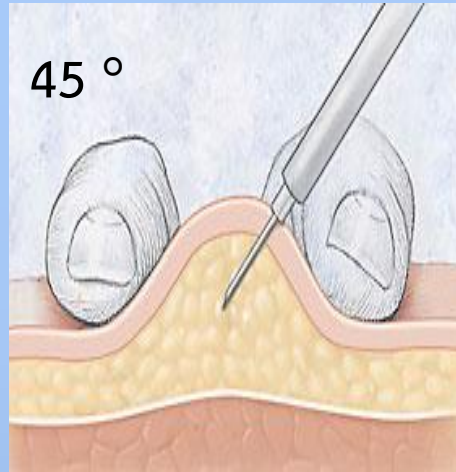
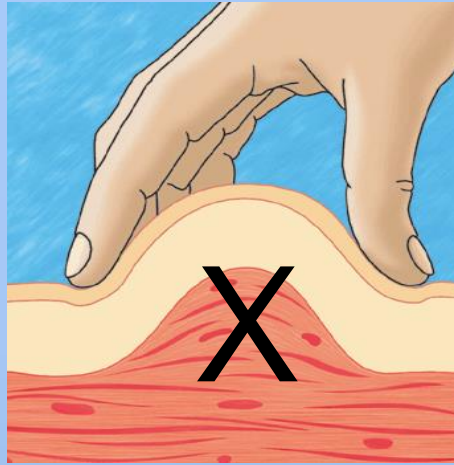
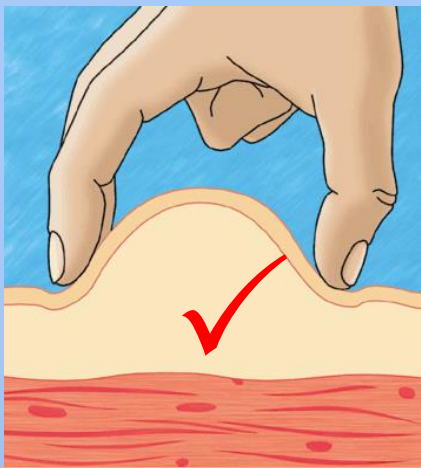


- **Wash your hands & allow to dry before applying latex gloves**
- **Scrub skin an injection site with 70% alcohol or 2%HCG in 70 % alc. (friction motion) allow to air dry for 30 sec**

Pertuzumab/Trastuzumab (phesgo) SC administration



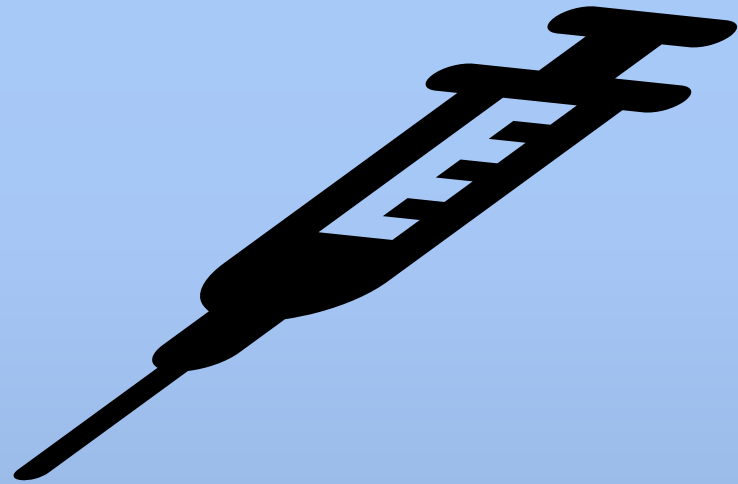
- Pinch the skin to separate subcutaneous layer and muscular layer



- Hold a syringe between thumb & forefinger of a dominant hand
- Insert the needle into skin of 45° / 90 °
“No need to draw back to test blood return
because of less blood flow”
- Push drug slowly 5-8 min depend on dosage



**Go to sharing technique for
High-Volume SC administration VDO Presentation**



Thank you