Indication	The first line treatment of locally advanced or metastatic breast cancer in patients whose tumours significantly overexpress HER2 at the 3+ level or FISH positive. NB Any adjuvant HER2 therapy must have been completed more than 12 months prior to diagnosis of locally advanced or metastatic disease.
Treatment Intent	Palliative
Frequency and number of cycles	Pertuzumab/trastuzumab SC and docetaxel every 3 weeks for 6 cycles (or more at clinician discretion) then continue pertuzumab / trastuzumab until unacceptable toxicity or visceral progression. NB patients can be switched between combination SC therapy (Phesgo®) or pertuzumab and trastuzumab IV therapy if the clinical need arises with the usual dosing interval.
Monitoring Parameters pre-treatment	• This regimen is restricted to patients whose tumours significantly overexpress HER2 at the 3+ level or FISH positive. • Monitor FBC, U&E and LFT at each cycle (cycles1-6). If neuts 1.0-1.4 and PLT >/=100 d/w consultant. If neuts >/= 1.5 and PLT >/= 100 continue with treatment. If neuts <1.0 or PLT <100 defer 1 week. (NB Pertuzumab/trastuzumab SC should not be reduced). • FBC, U&Es and LFTs should be monitored every 3 months or as clinically indicated from cycle 7 onwards. • **Renal and hepatic impairment:** Docetaxel not recommended in severe hepatic impairment. A dose reduction of docetaxel may be made dependent on PS and liver function. Dose reductions of pertuzumab/trastuzumab SC are not required in mild to moderate renal impairment. There are no recommendations for dose reductions in severe renal impairment or hepatic impairment. • At each nurse assessment patients should be assessed for signs of dyspnoea. • **Cardiac monitoring:** Cardiac function should be monitored at baseline (ECHO/MUGA and ECG), and every 12 weeks (ECHO or MUGA) during treatment or as clinically indicated. Patients should have a pre-treatment left ventricular ejection fraction (LVEF) of ≥ 50 %. Record on cardiac monitoring record on KOMs. It is the prescribers' responsibility to check that the ECHO/MUGA result is satisfactory before continuing treatment. If signs of left ventricular dysfunction see SPC and algorithm for continuation and discontinuation of pertuzumab/trastuzumab SC based on LVEF assessments. • **Re-loading:** The loading doses of pertuzumab/trastuzumab SC should be repeated if the interval between injections is 6 weeks or more (i.e. if the doses are missed by 3 weeks or more), thereafter the maintenance dose can be given. NB This applies regardless of whether prior treatment was pertuzumab iv and trastuzumab iv or pertuzumab / trastuzumab SC • **Pertuzumab/trastuzumab SC: Injection duration and monitoring:** The loading dose of pertuzumab/trastuzumab SC should be administered over 8 minutes, and the maintenance dose over 5 minutes. Patients must be observed closely for injection related adverse effects during administration and for 30 minutes after the completion of the loading dose of pertuzumab/trastuzumab SC and for 15 minutes after the completion of maintenance doses. If a significant injection-related reaction occurs, the injection should be slowed down or paused and appropriate medical therapies should be administered. Patients should be evaluated and carefully monitored until complete resolution of signs and symptoms. Discontinue pertuzumab/ trastuzumab SC in the event of grade 4 hypersensitivity reaction.

	• **Docetaxel:** Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel. • **<u>Administration of pertuzumab/trastuzumab SC</u>** • Inject into the subcutaneous tissue of the thigh only. Injection sites should alternate between left and right thigh. New injections should be given at least 2.5 cm from the previous site. Do not inject at other sites of the body. • Pertuzumab/trastuzumab solution for subcutaneous injection should never be injected into areas where the skin is red, bruised, tender, or hard. • The dose should not be split between two syringes or between two sites of administration. • During treatment with pertuzumab/trastuzumab solution for subcutaneous injection, do not administer other medicinal products for subcutaneous use at the same site. • **<u>Dose reduction</u>** ○ **Docetaxel:** dose reduction of docetaxel should be considered if grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to </=grade 1. ○ No dose reductions are recommended for pertuzumab/trastuzumab SC. ○ In the event docetaxel treatment is discontinued pertuzumab/trastuzumab SC treatment may continue. • Ensure dexamethasone pre-medication (8mg bd for 3 days starting the day before docetaxel) is prescribed and given to the patient at new patient chat. • **Common drug interactions(for comprehensive list refer to BNF/SPC):** • Pertuzumab/trastuzumab SC: No formal drug interaction studies have been performed. Caution with other cardiotoxic drugs. • Docetaxel: Concomitant use with medicines which induce, inhibit or are metabolised by cytochrome P450-3A (eg ciclosporin, ketoconazole and erythromycin) may affect levels of docetaxel, use with caution. Avoid concomitant use with strong CYP3A4 inhibitors (eg ketoconazole, itraconazole, clarithromycin and ritonavir), if treatment cannot be avoided consider dose reduction of docetaxel and monitor patient closely for signs of toxicity. • **Severe allergic reactions to docetaxel** • If a patient commences 1st line treatment with docetaxel and has a severe allergic reaction to docetaxel and is then re-challenged unsuccessfully with docetaxel, they may receive paclitaxel, pertuzumab / trastuzumab SC. The dosing schedule of paclitaxel is 80mg/m2 IV on days 1, 8 and 15 of a 21 day cycle. Patients should receive a total of 6 cycles or more of taxane based treatment. Paclitaxel (together with support medication) should be administered as per the KMCC BRE-036 protocol.
References	BRE-032 KMCC SACT proforma v6 (cycle 1 v5) SPC accessed online 08.01.21 BNF accessed online 11.01.21 Blueteq form accessed online 22.02.21 Roche medical information "Switching Between Perjeta with Herceptin and Phesgo" guidance letter received via email 13.01.21

NB For funding information, refer to CDF and NICE Drugs Funding List

Cycle 1: 21 days

Day	Drug	Dose	Route	Infusion/ Injection Duration	Administration
1	**Phesgo® (pertuzumab/ trastuzumab)**	**1200mg pertuzumab /600mg trastuzumab**	SC	8 minutes	Inject 15 mL into the subcutaneous tissue of the left or right thigh over 8 minutes. Do not inject at other sites of the body. Injection sites should be rotated for successive injections.
	Patients should be observed for injection-related reactions and hypersensitivity reactions for **30 minutes** following administration of Phesgo®, observation should be completed prior to any subsequent administration of chemotherapy.				
	Metoclopramide	20mg	IV		
	DOCETAXEL	**75mg/m²**	IV	1 hour	Sodium Chloride 0.9% 250ml
TTO	Drug	Dose	Route	Directions	
	Metoclopramide	10mg	PO	3 times a day for 3 days, then 10mg up to TDS when required (max. 30mg per day including 20mg pre-chemo dose). Do not take for more than 5 days continuously.	
	Dexamethasone	8mg	PO	BD for 3 days, starting day before next cycle of docetaxel.	

Cycle 2-6: repeat every 21 days

Day	Drug	Dose	Route	Infusion/ Injection Duration	Administration
1	**Phesgo® (pertuzumab/ trastuzumab)**	**600mg pertuzumab /600mg trastuzumab**	SC	5 minutes	Inject 10 mL into the subcutaneous tissue of the left or right thigh over 5 minutes. Do not inject at other sites of the body. Injection sites should be rotated for successive injections.
	Patients should be observed for injection-related reactions and hypersensitivity reactions for **15 minutes** following administration of Phesgo®, observation should be completed prior to any subsequent administration of chemotherapy.				
	Metoclopramide	20mg	IV		
	DOCETAXEL	**(75mg/m²)* (100mg/m²)***	IV	1 hour	Sodium Chloride 0.9% 250ml
	***The dose of docetaxel can be increased from 75mg/m² to 100mg/m² from cycle 2 onwards if patient is able to tolerate an increase in dose.**				

TTO	Drug	Dose	Route	Directions
	Metoclopramide	10mg	PO	3 times a day for 3 days, then 10mg up to TDS when required (max. 30mg per day including 20mg pre-chemo dose). Do not take for more than 5 days continuously.
	Dexamethasone	8mg	PO	BD for 3 days, starting day before next cycle of docetaxel.

Cycle 7 onwards: repeat every 21 days.

Day	Drug	Dose	Route	Injection Duration	Administration
1	**Phesgo® (pertuzumab/ trastuzumab)**	**600mg pertuzumab/600mg trastuzumab**	SC	5 minutes	Inject 10 mL into the subcutaneous tissue of the left or right thigh over 5 minutes. Do not inject at other sites of the body. Injection sites should be rotated for successive injections.
	Patients should be observed for injection-related reactions and hypersensitivity reactions for **15 minutes** following administration of Phesgo®				

Algorithm for Continuation and Discontinuation of Pertuzumab and Trastuzumab based on LVEF assessment