SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

TCHP
Docetaxel, Carboplatin, Trastuzumab, Pertuzumab Neoadjuvant protocol and continuation of Adjuvant Trastuzumab,Pertuzumab

PROTOCOL REF: MPHATCHP
(Version No. 2.3)

Approved for use in:

Neoadjuvant treatment: first line treatment of HER2 positive T2 to T4b and/or histologically or cytologically proven node positive early breast cancer.

Baseline LVEF ≥ 50%

Adjuvant treatment:

In combination with chemotherapy for HER2 positive, node positive early breast cancer.

or

Following neoadjuvant treatment (as detailed) and ONLY if fulfills one of the following criteria:

- Axillary lymph node (LN) involvement pathologically confirmed prior to the start of neoadjuvant chemotherapy.
- Node negative prior to neoadjuvant treatment:
    - Confirmed residual carcinoma in the axillary node(s) following surgery.
    - In the absence of invasive carcinoma in the axillary LNs post-surgery, confirmed histological changes (e.g. fibrosis) indicative of previous axillary nodal involvement.
    - No disease progression following neoadjuvant treatment.
    - Prior to starting adjuvant treatment LVEF ≥ 50%.
    - PS 0-1

****Separate Blueteq registration forms required for neoadjuvant and adjuvant use****

Preparation of Phesgo:

Loading Dose (Pertuzumab/Trastzumab S/C 1200mg/600mg)
Withdrawn the contents of the vial into a 15mL syringe using a transfer needle and then change the needle to a subcutaneous 25-27 Gauge needle prior to administering the dose

Maintenance Dose (Pertuzumab/Trastzumab S/C 600mg/600mg)
Withdrawn the contents of the vial into a 10mL syringe using a transfer needle and then change the needle to a subcutaneous 25-27 Gauge needle prior to administering the dose

Considerations

- The injection site should be alternated between the left and right thigh.
- Ensure both nursing staff and patient are in comfortable position before beginning
- New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard.
- Medication should be warmed/come to room temperature before injection. This is easily done by asking patient to hold vial of Phesgo while nurse performs assessment/documentation. Never injection cold medication into the patient
- The dose should not be split between two syringes or between two sites of administration

Dosage:

Drug	Dosage	Route	Frequency
Carboplatin*	AUC 5 or 6	IV infusion	Cycles 1 to 6 Day 1 only of a 21 day cycle
Docetaxel	75mg/m^2	IV infusion	Cycles 1 to 6 Day 1 only of a 21 day cycle
OR			
Paclitaxel	80mg/m^2	IV infusion	Cycles 1 to 6 Days 1, 8 and 15 of a 21 day cycle
Phesgo	Pertuzumab 1200mg/ Trastuzumab 600mg	Subcutaneous injection	Cycle 1 loading dose

Phesgo	Pertuzumab 600mg/ Trastuzumab 600mg	Subcutaneous injection	Cycles 2 to 6

Alternative intravenous option

Drug	Dosage	Route	Frequency
Trastuzumab	8mg/kg loading dose cycle 1 then 6mg/kg cycles 2 to 6	IV infusion	Cycles 1 to 6 Day 1 only of a 21 day cycle
Pertuzumab	840mg loading dose cycle 1 then 420mg cycles 2 to 6	IV infusion	

***Carboplatin Dosing**

Meditech calculates creatinine clearance using the Wright formula and therefore creatinine clearance will need to be entered manually to use Cockroft and Gault formula (applications for calculating creatinine using both formulas are available on the Remote Citrix Web Portal).

Calvert formula for Carboplatin dosage-:

Carboplatin dose in mg = AUC x (GFR or CrCl + 25)

Use area under the curve (AUC) 5 for GFR calculations using Wright formula and AUC 6 when using Creatinine Clearance (CrCl) using Cockroft and Gault formula. This formula will then need to be used throughout the course of carboplatin treatment.

If estimated GFR is used the **Wright formula** must be used for creatinine clearance.

In both cases carboplatin dose will be capped at 890mg.

Adjuvant treatment:

As 18 cycles of HER2 agents will be administered, ensure that cycle numbers are correct when starting adjuvant treatment to avoid stopping sooner than planned.

Eligible for adjuvant treatment with Pertuzumab

Drug	Dosage	Route	Frequency
Phesgo	Pertuzumab 1200mg/ Trastuzumab 600mg	Subcutaneous injection	Loading dose required if 6 weeks from previous dose Cycles 7 to 18 Day 1 only of a 21 day cycle
Phesgo	Pertuzumab 600mg/ Trastuzumab 600mg	Subcutaneous injection	

Intravenous alternative

Drug	Dosage	Route	Frequency
Trastuzumab	8mg/kg loading dose (≥ 6 weeks from last dose) cycle 8. Then 6mg/kg to continue thereafter for a total of 18 doses	IV infusion	Cycles 7 to 18 Day 1 only of a 21 day cycle
Pertuzumab	840mg loading dose (≥ 6 weeks from last dose) cycle 8. Then 420mg thereafter for a total of 18 doses	IV infusion	

Not eligible for adjuvant treatment with Pertuzumab:

Drug	Dose	Route	Frequency
Trastuzumab	600mg To continue for 18 doses in total	SC	Cycles 7 to 18 Day 1 only of a 21 day cycle

Administration:

Consider IV access, PICC line insertion is recommended for this regimen

See above for information on PHESGO administration

Emetogenic risk:

Moderately emetogenic.

Supportive treatments:

- Premedication of dexamethasone 8 mg oral twice daily for 3 days starting 1 day **prior to docetaxel administration** to prevent hypersensitivity reactions*
- Ondansetron 16mg PO or 8mg IV day 1 of treatment.
- Metoclopramide 10mg tablets orally three times a day when required, maximum 5 consecutive days.
- Filgrastim subcutaneous injection daily for 7 days starting on day 3, dose as follows with the docetaxel option:
    - Weight < 70kg Filgrastim 300 micrograms daily SC.
    - Weight ≥ 70kg Filgrastim 480 micrograms daily SC.

*If oral dexamethasone has not been taken then an intravenous dose of 8mg can be administered on the day of treatment, in addition to the oral dose of 8mg

Extravasation risk:

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'.

Docetaxel – exfoliant

Carboplatin – irritant

Trastuzumab – neutral

Pertuzumab – neutral

Paclitaxel- vesicant

Phesgo- No extravasation risk as subcutaneous route of injection

Dosing in renal and hepatic impairment:

Patients with creatinine clearance values of less than 60 mL/min are at greater risk to develop myelosuppression.

NB: If adjuvant zoledronate treatment is given in combination and renal function has dropped below 60ml/min then do not administer the zoledronate until the patients clinical team have reviewed the results and confirmed it is appropriate to continue.

Renal	Carboplatin	The optimal use of Carboplatin in patients presenting with impaired renal function requires adequate dosage adjustments and frequent monitoring of both haematological nadirs and renal function. Carboplatin is contraindicated if GFR or CrCl ≤ 20 ml/min. Do not give carboplatin and discuss with Oncologist.
	Pertuzumab, trastuzmab, docetaxel and paclitaxel	All grades including patients on haemodialysis - no dose adjustment required.

Hepatic	Pertuzumab, trastuzmab and carboplatin	No need for dose adjustment is required.	
	Docetaxel	**Docetaxel**	
		AST and/or ALT > 1.5 to 5 x ULN concomitant with ALP > 2.5 to 5.0 x ULN and normal bilirubin	Consider 75% of the original dose
		AST or ALT >1.5 to 5 x ULN concomitant with ALP ≤ 2.5 to 6 x ULN and/or bilirubin ≤ 1 to 1.5 x ULN	Consider 50% of the original dose
		Bilirubin > 1.5 x ULN or AST/ALT > 10 x ULN or ALP > 6 x ULN	Not recommended

	Paclitaxel	**Paclitaxel**
		Bilirubin less than 1.25 times ULN and AST < 10 x ULN: Give 100% dose
		Bilirubin greater than 1.25 times ULN: Consider dose reduction
		ALP more than 3 times ULN: Consider dose reduction
		ALT and/or AST ≥10 x ULN or bilirubin > 5 x ULN: Contra-.indicated

Interactions:

For detailed list of interactions please refer to the relevant SmPC

Treatment schedule:

Cycle 1

Carboplatin, Docetaxel and subcutaneous Trastuzumab/Pertuzumab

Day	Drug	Dose	Route	Diluent and rate
Dexamethasone* 8 mg twice daily for 3 days starting 1 day prior to docetaxel				
1	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Phesgo	Pertuzumab 1200mg/ trastuzumab 600mg	S/C injection	Over 8 minutes
	Docetaxel	75mg/m^2	IV	250mL 0.9% sodium chloride over 60 minutes
	Carboplatin	AUC 5 or 6	IV	500mL glucose 5% over 60 minutes

Carboplatin, Docetaxel, Trastuzumab, Pertuzumab intravenous

Day	Drug	Dose	Route	Diluent and rate
Dexamethasone* 8 mg twice daily for 3 days starting 1 day prior to docetaxel				
1	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Pertuzumab	**840mg Loading Dose**	**IV**	**250mL sodium chloride 0.9% over 60 minutes**
	Trastuzumab	**8mg/kg Loading Dose**	**IV**	**250mL sodium chloride 0.9% over 90 minutes**
	Docetaxel	**75mg/m^2**	**IV**	**250mL 0.9% sodium chloride over 60 minutes**
	Carboplatin	**AUC 5 or 6**	**IV**	**500mL glucose 5% over 60 minutes**

*If oral dexamethasone has not been taken then an intravenous dose of 8mg can be administered on the day of treatment, in addition to the oral dose of 8mg

OR

Paclitaxel, Carboplatin and subcutaneous Trastuzumab/Pertuzumab

Day	Drug	Dose	Route	Diluent and rate
1	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Phesgo	Pertuzumab 1200mg/ trastuzumab 600mg	S/C injection	Over 8 minutes
	Dexamethasone	6.6mg	IV Bolus	30 minutes before chemotherapy Reduce to 3.3mg from week 2
	Chlorphenamine	10mg	IV Bolus	30 minutes before chemotherapy

	Paclitaxel	80mg/m^2	IV infusion	250 to 500mL sodium chloride 0.9% over 60 minutes using a non-PVC giving set with a 0.22 micron filter
	Carboplatin	AUC 5 or 6	IV	500mL glucose 5% over 60 minutes

Paclitaxel, Carboplatin,Trastuzumab, Pertuzumab intravenous

Day	Drug	Dose	Route	Diluent and rate
1	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Pertuzumab	840mg Loading Dose	IV	250mL sodium chloride 0.9% over 60 minutes
	Trastuzumab	8mg/kg Loading Dose	IV	250mL sodium chloride 0.9% over 90 minutes
	Dexamethasone	6.6mg	IV Bolus	30 minutes before chemotherapy Reduce to 3.3mg from week 2
	Chlorphenamine	10mg	IV Bolus	30 minutes before chemotherapy
	Paclitaxel	80mg/m^2	IV infusion	250 to 500mL sodium chloride 0.9% over 60 minutes using a non-PVC giving set with a 0.22 micron filter
	Carboplatin	AUC 5 or 6	IV	500mL glucose 5% over 60 minutes

Cycle 2 to 6

Carboplatin, Docetaxel and subcutaneous Trastuzumab/Pertuzumab

Day	Drug	Dose	Route	Diluent and rate
Dexamethasone* 8 mg twice daily for 3 days starting 1 day prior to docetaxel				
1	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Phesgo	Pertuzumab 600mg/ trastuzumab 600mg	S/C injection	Over 5 minutes
	Docetaxel	75mg/m^2	IV	250mL 0.9% sodium chloride over 60 minutes
	Carboplatin	AUC 5 or 6	IV	500mL glucose 5% over 60 minutes

Carboplatin, Docetaxel, Trastuzumab, Pertuzumab intravenous

Day	Drug	Dose	Route	Diluent and rate
Dexamethasone* 8 mg twice daily for 3 days starting 1 day prior to docetaxel				
1	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Pertuzumab	420mg Maintenance Dose	IV	250mL sodium chloride 0.9% over 30 minutes
	Trastuzumab	6mg/kg Maintenance Dose	IV	250mL sodium chloride 0.9% over 60 minutes at cycle 2 then over 30 minutes if tolerated
	Docetaxel	75mg/m^2	IV	250mL 0.9% sodium chloride over 60 minutes
	Carboplatin	AUC 5 or 6	IV	500mL glucose 5% over 60 minutes

*If oral dexamethasone has not been taken then an intravenous dose of 8mg can be administered on the day of treatment, in addition to the oral dose of 8mg

OR

Paclitaxel, Carboplatin and subcutaneous Trastuzumab/Pertuzumab

Day	Drug	Dose	Route	Diluent and rate
1	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Phesgo	Pertuzumab 600mg/ trastuzumab 600mg	S/C injection	Over 5 minutes
1,8 And 15	Dexamethasone	6.6mg	IV Bolus	30 minutes before chemotherapy Reduce to 3.3mg from week 2
	Chlorphenamine	10mg	IV Bolus	30 minutes before chemotherapy
	Paclitaxel	80mg/m^2	IV infusion	250 to 500mL sodium chloride 0.9% over 60 minutes using a non-PVC giving set with a 0.22 micron filter
1	Carboplatin	AUC 5 or 6	IV	500mL glucose 5% over 60 minutes

Paclitaxel, Carboplatin,Trastuzumab, Pertuzumab intravenous

Day	Drug	Dose	Route	Diluent and rate
1	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Pertuzumab	840mg Loading Dose	IV	250mL sodium chloride 0.9% over 60 minutes
	Trastuzumab	8mg/kg Loading Dose	IV	250mL sodium chloride 0.9% over 90 minutes
1,8 and 15	Dexamethasone	6.6mg	IV Bolus	30 minutes before chemotherapy Reduce to 3.3mg from week 2
	Chlorphenamine	10mg	IV Bolus	30 minutes before chemotherapy
	Paclitaxel	80mg/m^2	IV infusion	250 to 500mL sodium chloride 0.9% over 60 minutes using a non-PVC giving set with a 0.22 micron filter
1	Carboplatin	AUC 5 or 6	IV	500mL glucose 5% over 60 minutes

Cycle 7 to 18

To commence 3 weeks after final cycle of chemotherapy (cycle 7 may be before surgery has taken place).

Adjuvant pertuzumab treatment

Subcutaneous

Drug	Dosage	Route	Frequency
Phesgo	Pertuzumab 1200mg/ Trastuzumab 600mg	Subcutaneous injection	Over 8 minutes **Loading dose required ONLY if 6 weeks from previous dose**
Phesgo	Pertuzumab 600mg/ Trastuzumab 600mg	Subcutaneous injection	Over 5 minutes

OR

Intravenous

Day	Drug	Dose	Route	Diluent and rate
1	Pertuzumab	840mg loading dose (≥ 6 weeks from last dose) cycle 7. Then 420mg thereafter for a total of 18 doses	IV infusion	250mL sodium chloride 0.9% over 60 minutes. If well tolerated then reduce to 30 minutes on subsequent infusions.
	Trastuzumab	8mg/kg loading dose (≥ 6 weeks from last dose) cycle 7. Then 6mg/kg to continue thereafter for a total of 18 doses	IV infusion	250mL sodium chloride 0.9% over 90 minutes. If well tolerated then reduce to 30 minutes on subsequent infusions.

OR

Adjuvant trastuzumab treatment ONLY

Day	Drug	Dose	Route	Diluent and rate
1	Trastuzumab	600mg	SC	Over 5 minutes

Cycles repeated every 21 days

Main toxicities:

TCH-P	
Haematological	Neutropenia, thrombocytopenia and anaemia.
Gastrointestinal	Nausea, vomiting, stomatitis, diarrhoea, mucositis.
Cardiotoxicity	Pertuzumab and Trastuzumab - decreases in LVEF have been reported with medicinal products that block HER2 activity, including Pertuzumab and Trastuzumab; see cardiotoxicity dose modification section below for details.
Dermatological	Alopecia, normally reversible, although can be permanent following docetaxel. Docetaxel: Brittle, chipped and ridged nails
Urological	Carboplatin is nephrotoxic.
Ototoxicity	Common when carboplatin used in high doses.
Ocular	Watery eyes, gritty and irritated. Risk of cortical blindness with carboplatin; renal impairment is thought to increase this risk.
Hypersensitivity reactions	Reactions may occur within a few minutes following the initiation of treatment with docetaxel, facilities for the treatment of hypotension and bronchospasm should be available. If hypersensitivity reactions occur, minor symptoms such as flushing or localised rash with or without pruritus do not require interruption of therapy. However, severe reactions, such as severe hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate treatment. Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel. Patients should be monitored for hypersensitivity and infusion reactions with Pertuzumab for 60 minutes after the first dose, and for 30 minutes after subsequent doses. Trastuzumab: Infusion reactions, allergic-like reactions and hypersensitivity can occur. The majority of these events occur during or within 2.5 hours of the start of the first infusion. Should an infusion reaction occur the infusion should be discontinued or the rate of infusion slowed and the patient should be monitored until resolution of all observed symptoms.

	Patients experiencing dyspnoea at rest may be at increased risk of a fatal infusion reaction; these patients should not be treated with Trastuzumab.
Nervous system	Taxanes: peripheral neuropathy is very common
Musculoskeletal	Arthralgia, myalgia common with Taxanes.
Infertility	Amenorrhea, risk of premature menopause However ensure appropriate contraceptive advice is given

Investigations and treatment plan

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	X				
Clinical Assessment All patients on SACT should have **at least one F2F review during treatment.**	X			X	As clinically indicated
SACT Assessment (to include PS and toxicities)	X	X	X	X	Every cycle
FBC	X	X	X	X	Every cycle of chemotherapy
U&E & LFTs & Magnesium	X	X	X	X	Every cycle of chemotherapy
CrCl (Cockcroft and Gault) and check carboplatin dose using the carboplatin calculator if on carboplatin	X	X	X	X	Every cycle of chemotherapy
ECG / ECHO	X				ECG and ECHO must be performed before pertuzumab and/or trastuzumab commences. Then every 4 months thereafter unless clinical suspicion of abnormal cardiac function
Blood pressure measurement	X				Repeat if clinically indicated
Weight recorded	X	X	X	X	Every cycle
Height recorded	X				

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

For paclitaxel option: on day 8 and 15 of the cycle if blood results do not meet the above levels the patient will miss that dose and proceed to the next cycle. Consider if filgrastim needed.

Second episode or severe neutropenic sepsis: Defer by 7 days or until blood counts recovered if Neutrophils ≤ 1.0 **or** platelets ≤ 100 x 10^9/L **and reduce** to 80% dose.

For pertuzumab/trastuzumab only cycles – no blood tests required

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity:

Peripheral Neuropathy

NCI-CTC grade 2 peripheral neuropathy: withhold taxane until neuropathy recovers to grade 1 then dose reduce by 20%

If NCI-CTC grade 3 (or persistent grade 2) peripheral neuropathy occurs, discontinue taxane.

Pulmonary Impairment:

Trastuzumab-Pulmonary events have been reported with the use of trastuzumab. These events have occasionally been fatal.

Caution should be exercised for pneumonitis.

Dose Modifications

Dose reductions for trastuzumab and pertuzumab are not recommended. If trastuzumab treatment is discontinued, treatment with Pertuzumab should be discontinued.

Recommendations regarding delayed or missed doses of trastuzumab and pertuzumab

Time between two sequential infusions	**Intravenous pertuzumab and trastuzumab**	**subcutaneous**	
		Phesgo	**trastuzumab single agent**
< 6 weeks	The 420 mg dose of intravenous pertuzumab should be administered as soon as possible. Do not wait until the next planned dose. Thereafter, revert to the original planned schedule.	The 600mg/600mg fixed dose should be administered as soon as possible	The fixed dose of 600mg trastuzumab SC should be administered as soon as possible. Do not wait until the next planned dose.
≥ 6 weeks	The 840 mg loading dose of intravenous pertuzumab should be re-administered as a 60 minute infusion, followed by a maintenance dose of 420 mg IV administered every 3 weeks thereafter.	The loading dose of 1200mg/600mg should be administered over 8 minutes and then back to 600mg/600mg maintenance dose every 3 weeks thereafter.	

Toxicities

Hypersensitivity

Taxanes- If hypersensitivity reactions occur; minor symptoms such as flushing or localised rash with or without pruritus do not require interruption of therapy. However, severe reactions, such as severe hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of taxane and appropriate treatment. Patients who have developed severe hypersensitivity reactions should not be re-challenged.

Should an infusion reaction occur the infusion should be discontinued. The symptoms should be managed using paracetamol, with addition of chlorphenamine and hydrocortisone if anaphylaxis suspected. Please refer to the trusts Hypersensitivity-Management Prevention Policy for full details.

Patient should be monitored until resolution of all observed symptoms. Patients experiencing dyspnoea at rest may be at increased risk of a fatal infusion reaction; these patients should not be treated with trastuzumab.

Cardiotoxicity

Management of Trastuzumab and Pertuzumab-Induced Cardiotoxicity (refer to NCRI recommendations 2009 outlined below)

- Sharp falls in LVEF (10 points or to <50%) during cytotoxic chemotherapy may indicate increased susceptibility to cardiac dysfunction on trastuzumab/pertuzumab. Prophylactic ACE inhibitor therapy may be considered for such patients.
- Assessment at the end of treatment is recommended for patients requiring cardiovascular intervention during treatment.
- Additional testing is required in patients who have LV systolic dysfunction.
- Patients developing signs and symptoms of heart failure should have their trastuzumab/pertuzumab treatment interrupted, receive an ACE inhibitor and be referred to a cardiologist.
- If the LVEF falls to ≤ 40%, (representing biologically important LV systolic dysfunction) trastuzumab/pertuzumab should be interrupted the patient should receive an ACE inhibitor and be referred to a cardiologist for treatment.

- After trastuzumab interruption and appropriate medical therapy, LVEF should be re-checked after 6–8 weeks. Trastuzumab may be re-initiated if the LVEF is restored to a level above the LLN.
- If the LVEF falls to below the LLN but > 40%, trastuzumab may be continued, but an ACE inhibitor should be initiated.
- If the patient is already on an ACE inhibitor, they should be referred to a cardiologist.
- LVEF assessment should be repeated after 6–8 weeks.
- If the LVEF falls by 10 points or more but remains above the LLN, trastuzumab may be continued. Intervention with an ACE inhibitor is recommended in an attempt to reduce the risk of further LVEF decline of symptomatic CHF.
- LVEF Monitoring should be repeated after 6–8 weeks.

NCRI recommendations for cardiac monitoring
Ref: British Journal of Cancer 2009 100:684-692

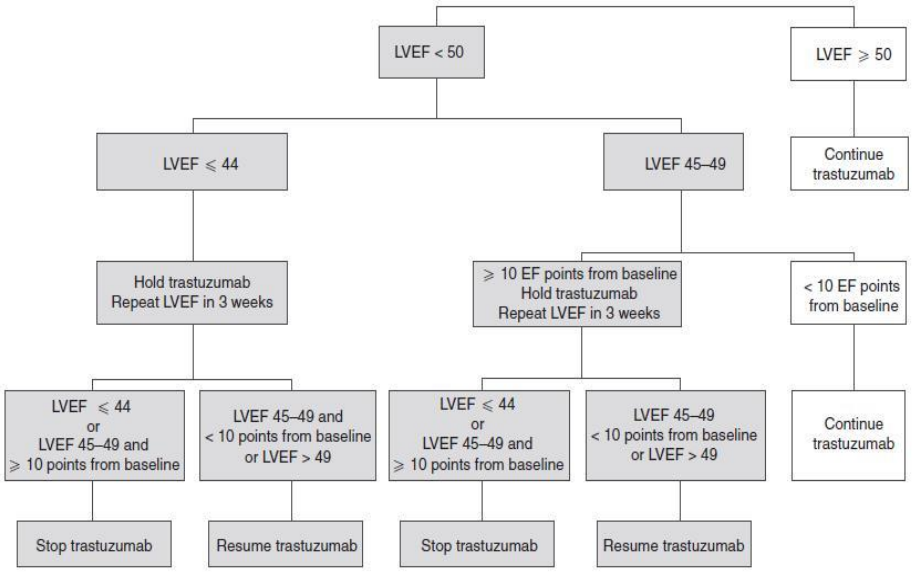

Figure 1 Current recommendations for cardiac monitoring in trastuzumab-treated patients (reproduced from Suter *et al*, 2007; online Appendix only). Reproduced with permission of the American Society of Clinical Oncology, from Suter *et al*, 2007.

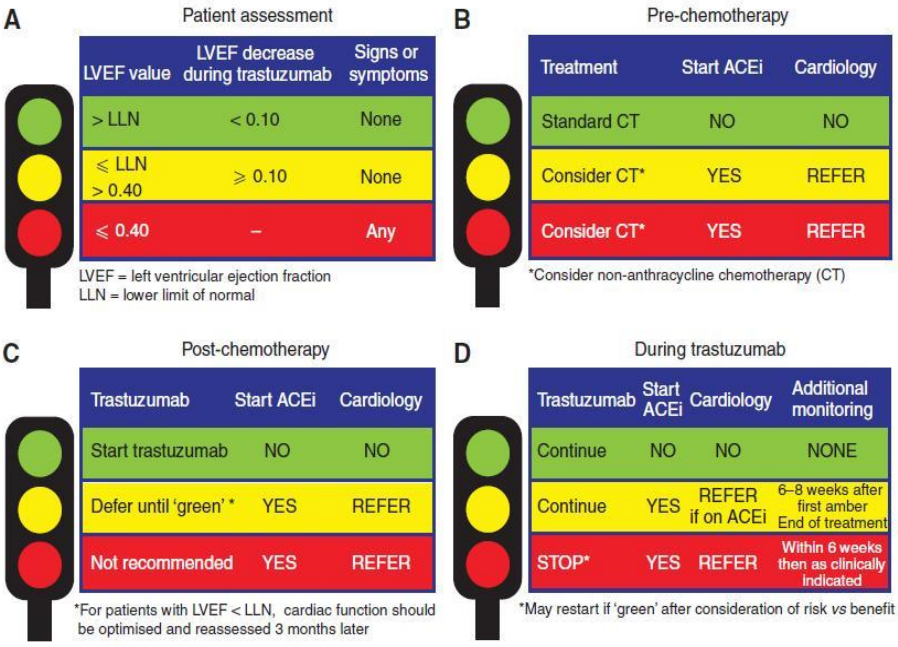

Figure 2 Traffic light system to prevent, monitor, and manage cardiac events in patients undergoing cytotoxic chemotherapy. (**A**) Patient assessment during trastuzumab therapy; (**B**–**D**) indications for ACEi therapy and referral to a cardiologist before (**B**) and after (**C**) chemotherapy, and (**D**) during trastuzumab therapy, when additional cardiac assessments may also be required. ACEi = angiotensin-converting enzyme inhibitor.

References:

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3. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.
4. APHINITY trial results, NEJM 2017; 377:122-131
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Circulation/Dissemination

Date added into Q-Pulse	For completion by DCM
Date document posted on the Intranet	For completion by DCM

Version History

		Author name and designation	Summary of main changes
		Gabby Langton and Helen Flint	Transferred to new format
		Gabriella Langton	**Removal of famotidine, addition of zolendronic acid renal information, added reminder for F2F reviews**