DOCETAXEL CARBOPLATIN PERTUZUMAB / TRASTUZUMAB (Phesgo) SC (adjuvant)

INDICATION (ICD10) C50

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (PER2b)

1. Pertuzumab in combination with intravenous trastuzumab and chemotherapy as adjuvant therapy for axillary node positive HER2-positive (HER2 3+), adequately excised early breast cancer and with NO preceding neoadjuvant chemotherapy in combination with pertuzumab and trastuzumab. PS 0 or 1. (TA569)

REGIMEN

Drugs can be given on any day ie 1 or 2. When given in combination with a taxane on the same day the pertuzumab and trastuzumab should be administered 30 minutes before the taxane.

Cycle 1

Day 1 *PERTUZUMAB with TRASTUZUMAB 1800mg SC over 8 minutes
(if previous neoadjuvant dose <6 weeks ago reduce dose to 1200mg maintenance dose)
(1800mg equivalent to pertuzumab 1200mg and trastuzumab 600mg (1200/600mg vial)).
Premedication: Dexamethasone 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg BD post-chemotherapy for 2 days

DOCETAXEL	75mg/m^2 in 250ml sodium chloride 0.9% IV infusion over 60 minutes
CARBOPLATIN	AUC 5 (if CrCl used maximum 700mg) in 500ml glucose 5% IV infusion over 30 minutes. Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC.

Cycles 2 to 6

Day 1 *PERTUZUMAB with TRASTUZUMAB 1200mg SC over 5 minutes
(1200mg equivalent to pertuzumab 600mg and trastuzumab 600mg (600/600mg vial)).
Premedication: Dexamethasone 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg BD post-chemotherapy for 2 days

DOCETAXEL	75mg/m^2 in 250ml sodium chloride 0.9% IV infusion over 60 minutes
CARBOPLATIN	AUC 5 (if CrCl maximum 700mg) in 500ml glucose 5% IV infusion over 30 minutes Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC.

Cycles 7 to 18

Day 1 *PERTUZUMAB with TRASTUZUMAB 1200mg SC over 5 minutes
(1200mg equivalent to pertuzumab 600mg and trastuzumab 600mg (600/600mg vial)).

*For patients unable to receive SC pertuzumab / trastuzumab (phesgo) see the pertuzumab trastuzumab IV substitution regimen for IV pertuzumab plus IV trastuzumab doses, observation times etc.

Pertuzumab / Trastuzumab loading dose - observation time post injection 30 minutes
Pertuzumab / Trastuzumab maintenance doses - observation time post injection 15 minutes

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for 6 cycles
Pertuzumab with trastuzumab SC every 21 days from cycle 7 up to cycle 18

ANTI-EMETICS
Moderate risk day 1 cycles 1 to 6
Minimal risk day 1 cycles 7 to 18

CONCURRENT MEDICATION REQUIRED

Carboplatin	Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously. Dexamethasone 20mg IV bolus Chlorphenamine 10mg IV bolus H_2 antagonist Carboplatin should be given at a slower rate e.g. 2-4 hours.
Docetaxel	Ensure premedication given before docetaxel. This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions. Loperamide prn every docetaxel cycle
Pertuzumab with Trastuzumab	Infusion related chills and/or fevers – treat with paracetamol and chlorphenamine.
GCSF	GCSF to be added if delays / neutropenic sepsis.

EXTRAVASATION AND TYPE OF LINE / FILTERS
Carboplatin - irritant
Docetaxel – exfoliant

Filter not required
Central or peripheral line

INVESTIGATIONS
Blood results required before SACT administration:
FBC, U&E and LFTs cycles 1 to 6
FBC every 3 months cycles 7 to 18
Neutrophils x 10^9/L ≥1.0
Platelets x 10^9/L ≥100
Baseline weight and every cycle for cycles 1 to 6, then 3 monthly weight.
Monitor cardiac function according to network guidelines. Baseline LVEF greater than or equal to 55% or if anthracyclines were given that the LVEF was greater than or equal to 50% after completion of the anthracycline component of the adjuvant chemotherapy.

MAIN TOXICITES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
Docetaxel	Cutaneous reactions, peripheral neuropathy or fluid retention, hypersensitivity reactions
Pertuzumab with Trastuzumab	Cardiotoxicity - monitor cardiac function. Injection related chills, fevers or headache, slow the rate of injection or pause and appropriate medical therapies administered (Treatment including oxygen, beta agonists, antihistamines, rapid intravenous fluids and antipyretics may also help alleviate systemic symptoms). For severe injection related reactions discontinue permanently. Other symptoms may include nausea, hypertension, vomiting, pain, rigors, headache, cough, dizziness, rash, and asthenia. Febrile neutropenia, diarrhea, pulmonary events Cardiomyopathy: Pertuzumab with trastuzumab administration can result in subclinical and clinical cardiac failure manifesting as CHF, and decreased LVEF, with greatest risk when administered concurrently with anthracyclines. Evaluate cardiac function prior to and during treatment. Discontinue pertuzumab with trastuzumab for cardiomyopathy.

DOSE MODIFICATIONS

Pertuzumab with trastuzumab

Delay more than 6 weeks since last dose

The loading dose of pertuzumab with trastuzumab 1800mg SC (equivalent to pertuzumab 1200mg and trastuzumab 600mg (1200/600mg vial)) should be readministered for 1 dose
then followed by maintenance doses of pertuzumab with trastuzumab 1200mg SC (equivalent to pertuzumab 600mg and trastuzumab 600mg (600/600mg vial)).

Haematological

Docetaxel

In patients who experienced either febrile neutropenia, neutrophil count $<0.5x10^9$/L for more than one week, severe or cumulative cutaneous reactions or severe peripheral neuropathy during docetaxel therapy, the dose of docetaxel should be reduced from 75 to 60mg/m². If the patient continues to experience these reactions at 60mg/m², the treatment should be discontinued

Non-haematological

Docetaxel

Discuss dose reductions if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Pertuzumab with Trastuzumab

Continuation and discontinuation of pertuzumab with trastuzumab based on interval LVEF assessment as per network guidelines.

Hepatic impairment

Docetaxel

ALT and/or AST >1.5xULN and ALP >2.5xULN	SPC contains dose recommendations for 100mg/m^2 only therefore Clinician discretion
Bilirubin >ULN and ALT and AST >3.5xULN with ALP >6xULN	should not be used unless strictly indicated.

Renal impairment

Carboplatin

GFR / calculated CrCl ≤20ml/min or ≤30ml/min with pre-existing severe renal impairment	contraindicated

REFERENCES

1. APHINITY Trial NEJM 2017: 377:122-131