DOCETAXEL PERTUZUMAB / TRASTUZUMAB (Phesgo) SC (metastatic)

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/) (PER1)

1. The first line treatment of locally advanced or metastatic HER2 3+ breast cancer, where any adjuvant HER2 therapy was completed more than 12 months prior to the diagnosis of locally advanced or metastatic disease, in combination with docetaxel. PS 0 or 1. (TA509)

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
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

Cycles 2 to 6

Day 1 *PERTUZUMAB with TRASTUZUMAB 1200mg SC over 5 minutes
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

Cycle 7 onwards

Day 1 *PERTUZUMAB with TRASTUZUMAB 1200mg SC over 5 minutes

*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 every 21 days from cycle 7 continue until disease progression

ANTI-EMETICS

Low risk day 1 cycles 1 to 6
Minimal risk day 1 cycle 7 onwards

CONCURRENT MEDICATION REQUIRED

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.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Docetaxel – exfoliant

No filters 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 onwards
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Haemoglobin g/dL ≥10
Baseline weight and every cycle for cycles 1 to 6, then 3 monthly weight.
Monitor cardiac function according to network guidelines. Baseline LVEF of greater than or equal to 50%.

MAIN TOXICITES AND ADVERSE REACTIONS

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 and trastuzumab based on interval LVEF assessment as per network guidelines

Hepatic impairment
Docetaxel

ALT and/or AST >1.5xULN and ALP >2.5xULN	recommended SPC dose for 100mg/m^2 is give 75mg/m^2
Bilirubin >ULN and ALT and AST >3.5xULN with ALP >6xULN	should not be used unless strictly indicated.

REFERENCES
1. CLEOPATRA NEJM 2015 372(8): 724-34