DOCETAXEL CARBOPLATIN TRASTUZUMAB (Herceptin subcutaneous)

INDICATION (ICD10) C50

1. Adjuvant Her2 positive breast cancer, unsuitable for an anthracycline. PS 0, 1, 2

REGIMEN

Drugs can be given in any order

Cycles 1 to 6

Day 1 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.
*TRASTUZUMAB	600mg SC over 5 minutes

Cycles 7 to 18

Day 1 *TRASTUZUMAB 600mg SC over 5 minutes

*For patients unable to receive SC trastuzumab see the trastuzumab monotherapy regimen for IV trastuzumab doses, observation times etc.

Trastuzumab - observation time post injection 30 minutes after the first injection and for 15 minutes after subsequent injections.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for 6 cycles
Trastuzumab monotherapy every 21 days from cycle 7 up to cycle 18

ANTI-EMETICS

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

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
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
Trastuzumab SC– neutral

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
Monitor cardiac function according to network guidelines

MAIN TOXICITES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
Docetaxel	Cutaneous reactions, peripheral neuropathy or fluid retention, hypersensitivity reactions
Trastuzumab	Cardiotoxicity - monitor cardiac function. Trastuzumab infusion related chills and/or fevers are commonly observed during the first infusion (but infrequently with subsequent infusions). Other symptoms may include nausea, hypertension, vomiting, pain, rigors, headache, cough, dizziness, rash, and asthenia. Some adverse reactions to trastuzumab infusion including dyspnoea, hypotension, wheezing, bronchospasm, supraventricular tachyarrhythmia, reduced oxygen saturation and respiratory distress can be serious and potentially fatal. If symptoms of back ache, nausea or vomiting, do a set of obs. Give hydrocortisone 100mg IV, chlorphenamine 10mg IV.

DOSE MODIFICATIONS

Trastuzumab
If the patient misses a dose of Trastuzumab subcutaneous formulation, it is recommended to administer the next 600mg dose (i.e the missed dose) as soon as possible. The interval between consecutive Trastuzumab subcutaneous formulation administrations should not be less than three weeks.

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.

Trastuzumab
No dose reduction or cessation of trastuzumab is required if patient has acute reversible neutropenia.

Non-haematological

Docetaxel

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

Trastuzumab

Continuation and discontinuation of 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.

Renal impairment

Carboplatin

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

REFERENCES

1. Valero V, Forbes J, Pegram MD et al. Multicentre phase III randomised trial comparing docetaxel and trastuzumab with docetaxel, carboplatin and trastuzumab as first line chemotherapy for patients with HER2 positive gene amplified metastatic breast cancer (BCIRG007 study); two highly active therapeutic regimens. J Clin Oncol 2011; 29 (2): 149-15
2. Slamon, D et al; NEJM 2011; 365 (14): 1273–1283
3. Coudert, B et al; JCO 2007; 25 (19): 2678-2684