PACLITAXEL weekly TRASTUZUMAB (Herceptin subcutaneous)

INDICATION (ICD10) C50

1. Adjuvant HER 2+ve patient who is contraindicated to docetaxel following on from the anthracycline component of treatment (eg in EC-docetaxel). (Weekly schedule is unlicensed treatment).
2. Metastatic breast cancer not eligible for docetaxel pertuzumab trastuzumab (weekly paclitaxel is unlicensed treatment). PS 0, 1 or 2

REGIMEN

Cycles 1 to 4

Days 1, 8 and 15 Premedication 30 minutes prior to infusion:
Dexamethasone 8mg IV bolus
Chlorphenamine 10mg IV bolus
PACLITAXEL 80mg/m^2 in 250ml* sodium chloride 0.9% infusion over 60 minutes
Day 1 **TRASTUZUMAB 600mg SC over 5 minutes
* doses 162mg to 600mg in 500ml sodium chloride 0.9%

Cycles 5 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

Every 21 days
Adjuvant
Paclitaxel every 7 days for 9 to 12 weeks (3-4 x 21 days)
Trastuzumab monotherapy cycles 5 to 18
Metastatic
Paclitaxel every 7 days for 12 weeks (4 x 21 days)
Trastuzumab monotherapy until disease progression

ANTI-EMETICS

Low risk days 1, 8 and 15 cycles 1 to 3-4
Minimal risk day 1 cycles 5 onwards

CONCURRENT MEDICATION REQUIRED

Paclitaxel	Ensure premedication given before paclitaxel
Trastuzumab	Infusion related chills and/or fevers – treat with paracetamol and chlorphenamine.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Paclitaxel – vesicant

Administer paclitaxel via polyethylene lined administration set with ≤0.22micron filter
Central line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every week cycles 1 to 4
Neutrophils x 10^9/L ≥1.0 (adjuvant)
Neutrophils x 10^9/L ≥1.5 (metastatic)
Platelets x 10^9/L ≥100
Baseline weight and every cycle cycles 1 to 4
Monitor cardiac function according to network guidelines

MAIN TOXICITES AND ADVERSE REACTIONS

Paclitaxel	(2% risk of severe hypersensitivity) Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.
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.

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Paclitaxel	DOACs to be used with caution, need dose modifications or to be avoided eg apixaban Clopidogrel interacts with paclitaxel, potentially increasing the concentration of paclitaxel. Paclitaxel is catalysed, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. inhibitors (e.g. erythromycin, fluoxetine, gemfibrozil) use with caution. inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, efavirenz, nevirapine) use with caution.

DOSE MODIFICATIONS

Haematological

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

Non-haematological

Paclitaxel

If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration

If grade ≥2 neuropathy, consider giving 75% paclitaxel dose

If grade >3 peripheral neuropathy is >grade 3 omit further paclitaxel

Trastuzumab

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

Hepatic impairment

Paclitaxel

In the absence of Gilbert's syndrome:

Transaminase <10xULN and bilirubin ≤1.25xULN	no dose reduction
Transaminase <10xULN and bilirubin 1.26-2xULN	clinician discretion
Transaminase <10xULN and bilirubin 2·01-5xULN	clinician discretion
Transaminase ≥10xULN or bilirubin >5xULN	contraindicated

REFERENCES

1. Andrew D. Seidman, Donald Berry, Constance Cirrincione, Lyndsay Harris, Hyman Muss, P. Kelly Marcom, Grandella Gipson, Harold Burstein, Diana Lake, Charles L. Shapiro, Peter Ungaro, Larry Norton, Eric Winer and Clifford Hudis. JCO 2008. Randomized Phase III Trial of Weekly Compared With Every-3-Weeks Paclitaxel for Metastatic Breast Cancer, With Trastuzumab for all HER-2 Overexpressors and Random Assignment to Trastuzumab or Not in HER-2 Nonoverexpressors: Final Results of Cancer and Leukemia Group B Protocol 9840
2. Joseph A. Sparano, M.D., Molin Wang, Ph.D., Silvana Martino, D.O., Vicky Jones, M.D., Edith A. Perez, M.D., Tom Saphner, M.D., Antonio C. Wolff, M.D., George W. Sledge, Jr., M.D., William C. Wood, M.D., and Nancy E. Davidson, M.D. N Engl J Med. 2008 Apr 17; 358(16): 1663–1671. doi: 10.1056/NEJMoa0707056 Weekly Paclitaxel in the Adjuvant Treatment of Breast Cancer