PACLITAXEL CARBOPLATIN with concurrent RT

INDICATION (ICD10) C15

1. Oesophageal cancer chemo radiotherapy (unlicensed). PS 0, 1 or 2

REGIMEN

Drugs can be given in any order

Days 1, 8, 15, 22 and 29

Premedication 30 minutes prior to infusion:

Dexamethasone	8mg IV bolus
H_2 antagonist	
Chlorphenamine	10 mg IV bolus
PACLITAXEL	50mg/m^2 in 250ml sodium chloride 0.9% IV infusion over 60 minutes
CARBOPLATIN	AUC 2 in 500ml glucose 5% IV infusion over 30 minutes Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC. Maximum dose when using CrCl 125+25 x AUC

CYCLE FREQUENCY AND NUMBER OF CYCLES

One cycle

ANTI-EMETICS

Moderate risk days 1, 8, 15, 22 and 29

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.
Paclitaxel	Ensure premedication given before paclitaxel

EXTRAVASATION AND TYPE OF LINE / FILTERS

Carboplatin - irritant
Paclitaxel – vesicant

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

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs, creatinine every dose
Neutrophils x 10^9/L ≥1.5 (1-1.5 discuss with consultant)
Platelets x 10^9/L ≥100 (75-100 discuss with consultant)
GFR assessed using EDTA result or calculated creatinine clearance at the Consultant's discretion.
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
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.

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
Omit if neutrophil count <1.5x10^9/L and / or platelet count is <100x10^9/L on day of chemotherapy.

Non-haematological
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

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	give 77% of original dose
Transaminase <10xULN and bilirubin 2·01-5xULN	give 51% of original dose
Transaminase ≥10xULN or bilirubin >5xULN	contraindicated

Renal impairment
Carboplatin

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

REFERENCES