

## PACLITAXEL weekly CARBOPLATIN weekly CISPLATIN with concurrent RT

### INDICATION (ICD10) C53.9

1. Neoadjuvant cervical cancer

PS 0, 1 or 2

Weekly paclitaxel is unlicensed

### REGIMEN

#### Cycles 1 to 6

#### Drugs can be given in any order

Day 1 Premedication 30 minutes prior to infusion:

Dexamethasone 8mg IV bolus

Chlorphenamine 10mg IV bolus

PACLITAXEL 80mg/m<sup>2</sup>\* in #ml sodium chloride 0.9% IV infusion over 60 minutes

CARBOPLATIN AUC 2 in #ml glucose 5% IV infusion over 30 minutes

Dose calculated by EDTA GFR or calculated (CrCl + 25)\*\* x AUC.

#### Cycles 7 to 11

Day 1 Prehydration

CISPLATIN 40mg/m<sup>2</sup> (maximum 70mg) in 1000ml sodium chloride 0.9% IV infusion over 60 minutes

Post hydration

Cisplatin should be given as early as possible in the week as cisplatin potentiates the radiotherapy

# diluent volume for dose prescribed as per national standardised product specification

\* dose capped at BSA 2.0m<sup>2</sup>

\*\* dose capped at CrCl 110ml/min

### CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 7 days for 11 cycles

### ANTI-EMETICS

Moderate risk day 1

### 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 Carboplatin should be given at a slower rate e.g. 2-4 hours.
Cisplatin	Ensure adequate pre and post hydration. If urine output is <100ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.
Paclitaxel	Ensure premedication given before paclitaxel

## EXTRAVASATION AND TYPE OF LINE / FILTERS

Carboplatin - irritant  
Cisplatin – exfoliant  
Paclitaxel – vesicant

Administer paclitaxel via polyethylene lined or DEHP free administration set with  $\leq 0.22$ micron filter  
Central or peripheral line

## INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E including  $Mg^{++}$  and LFTs, creatinine day 1 Neutrophils  $\times 10^9/L \geq 1.5$

Platelets  $\times 10^9/L \geq 100$

GFR assessed using EDTA result or calculated creatinine clearance at the Consultant's discretion.

Baseline weight and every cycle

## MAIN TOXICITIES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.
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)

Cisplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Cisplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.
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

### Non-haematological

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

#### Paclitaxel

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

If grade  $\geq 2$  neuropathy, consider paclitaxel dose reduction

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

### Hepatic impairment

#### Paclitaxel

In the absence of Gilbert's syndrome:

Transaminase $<10$ xULN and bilirubin $\leq 1.25$ xULN	no dose reduction
Transaminase $<10$ xULN and bilirubin 1.26-2xULN	give 77% of original dose
Transaminase $<10$ xULN and bilirubin 2.01-5xULN	give 51% of original dose
Transaminase $\geq 10$ xULN or bilirubin $>5$ xULN	contraindicated

### Renal impairment

#### Carboplatin

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

#### Cisplatin

CrCl $>60$ ml/min	give 100% dose
CrCl 50-59ml/min	give 75% dose
CrCl 40-49ml/min	give 50% dose (curative intent)
CrCl $<40$ ml/min	not recommended

## REFERENCES

1. INTERLACE study