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 paclitaxel: Chlorphenamine 10mg IV bolus Dexamethasone 8mg IV bolus			
	PACLITAXEL	80mg/m^2	IV infusion	#ml sodium chloride 0.9% over 60 minutes
	CARBOPLATIN	AUC** 2	IV infusion	#ml glucose 5% over 30 minutes

Cycles 7 to 11

Day 1	Prehydration			
	CISPLATIN	40mg/m^2 (maximum 70mg)	IV infusion	#ml sodium chloride 0.9% 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^2
** dose calculated by EDTA GFR or calculated (CrCl + 25)** x AUC (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 H_2 antagonist 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 ≤0.22micron filter
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E including Mg^{++} (>0.4) and LFTs Neutrophils x 10^9/L ≥1.5 Platelets ≥100x10^9/L	baseline and every cycle
GFR assessed using EDTA result (BMI <19 or >30 or calculated creatinine clearance at the Consultant's discretion	baseline and every cycle
Serum creatinine	baseline and every cycle
CA125	baseline and day 1 every cycle
Audiology	baseline
Virology	before cycle 1 if not previously checked
Weight	baseline and every cycle

MAIN TOXICITES 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 ≥2 neuropathy, consider paclitaxel dose reduction
If grade >3 peripheral neuropathy is >grade 3 omit further paclitaxel

Hepatic impairment
Carboplatin
No need for dose adjustment is expected

Cisplatin
No need for dose adjustment is expected

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

Cisplatin

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

Paclitaxel
No need for dose adjustment is expected

REFERENCES

1. INTERLACE study

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Every cycle
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E, calcium, magnesium & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
CT scan	X					At cycle 6, Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle