Weekly Carboplatin and Paclitaxel (Cervix)

Indication

Short course weekly induction chemotherapy prior to concurrent cisplatin-radiotherapy in locally advanced cervical cancer.

ICD-10 codes

Codes prefixed with C53

Regimen details

Induction chemotherapy (weeks 1- 6)

Day	Drug	Dose	Route
1, 8, 15, 22, 29, 36	Paclitaxel	80 mg/m^2	IV infusion
1, 8, 15, 22, 29, 36	Carboplatin	AUC 2*	IV infusion

* Carboplatin dose calculated using the Calvert equation: **Carboplatin dose (mg) = AUC (CrCl +25)**
The creatinine clearance (CrCl) is calculated using the Cockcroft and Gault equation, however for patients where the creatinine level may not truly reflect renal function (e.g. in extremes of BSA or debilitated patients) a measured GFR should be performed.
CrCl should be capped at 125mL/min.

Cycle frequency

Weekly for 6 weeks

Number of cycles

As above.

Administration

Paclitaxel should be administered first. Paclitaxel is administered in a 250mL sodium chloride 0.9% non-PVC infusion bag with a 0.22 micron in-line filter over 1 hour. Blood pressure and pulse should be monitored regularly (e.g. every 30 minutes) during paclitaxel infusion.

Carboplatin should be administered in 250mL glucose 5% over 30 minutes.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of paclitaxel or carboplatin. Facilities for the treatment of hypotension and bronchospasm **must** be available. If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve re-started at a slower infusion rate. Chlorphenamine 10mg IV may be re-administered. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of paclitaxel or carboplatin and appropriate therapy initiated.

Pre-medication

30 minutes prior to each paclitaxel infusion.
Chlorphenamine 10mg IV slow bolus.
Dexamethasone 8mg IV slow bolus.

Emetogenicity

This regimen has moderate emetic potential.

Additional supportive medication

Proton pump inhibitor if required.
Loperamide if required.
Laxatives if required.
Mouthwashes as per local policy.

Extravasation

Carboplatin – irritant (Group 3).
Paclitaxel – vesicant (Group5).

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Calcium	14 days
Magnesium	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	Pre day 8, 15, 22, 29, 36. Results valid for 24 hours
U+E (including creatinine)	Pre day 22 i.e. 3 weekly during treatment. Results valid for 96 hours.
LFTs	Pre day 22 i.e. 3 weekly during treatment. Results valid for 96 hours.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 75 x 10^9/L
Bilirubin	< 1.5 x ULN
AST/ALT	< 5 x ULN
Creatinine Clearance (CrCl)	> 30 mL/min (and < 10% change in creatinine)

Dose modifications

- ### Haematological toxicity

If neutrophils < 1 x 10^9/L or platelets < 75 x 10^9/L on day of treatment, omit treatment and reduce paclitaxel to 70mg/m^2 and carboplatin to AUC 1.6 for future doses.

If further haematological toxicity despite dose reduction, discontinue treatment and proceed to chemo-radiation phase of treatment.

- **Renal impairment**

Paclitaxel: no dose adjustment is expected.
Carboplatin: If creatinine increases by 10% from baseline consider re-calculation of carboplatin dose. If CrCl is <30mL/min follow advice below:

CrCl (mL/min)	**Carboplatin dose**
> 30	100%
20-30	Measured GFR then 100% dose (or consider changing to non-nephrotoxic regimen, discuss with consultant)
< 20	Discuss with consultant

- **Hepatic impairment**

Paclitaxel

Hepatic function		**Paclitaxel dose**
Bilirubin	1.5 – 3 x ULN	50%
	> 3 x ULN	Discontinue
ALT / AST	>5 x ULN	Discontinue

Carboplatin – no need for dose adjustment expected. Consultant decision if bilirubin > 5 x ULN or ALT ≥ 10 x ULN.

- **Peripheral neuropathy**

Grade	**Carboplatin dose**	**Paclitaxel dose**
Grade 2	100%	75%
≥ Grade 3	75%	Discontinue

- **Other toxicities**

Any Grade 3-4 toxicity (except alopecia) – delay until ≤ Grade 1 toxicity and reduce dose to paclitaxel 70mg/m2 and Carboplatin AUC1.6.
Discuss with consultant.

Adverse effects - for full details consult product literature/ reference texts

- **Rare or Serious side effects**

Myelosuppression
Hypersensitivity reactions
Pulmonary fibrosis
Nephrotoxicity
Electrolyte disturbances
Arrhythmias
Cardiac failure
Febrile Neutropenia

- **Frequently occurring side effects**

Nausea and vomiting
Mucositis, stomatitis
Myelosuppression
Diarrhoea, constipation
Peripheral neuropathy
Oedema
Phlebitis

Myalgia, arthralgia
Alopecia
Fatigue

- **Other side effects**

Flu-like symptoms
Taste changes
Headache
Abdominal pain
Deranged liver function
Rash
Ototoxicity
Elderly patients may have a higher incidence of severe neuropathy, severe myelosuppression, or cardiovascular events compared to younger patients.

Significant drug interactions – for full details consult product literature/ reference texts

Additional comments

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin or DOAC during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Clozapine: increased risk of agranulocytosis, avoid concomitant use.

Paclitaxel is a CYP 2C8 and CYP 3A4 substrate. Drug levels may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

Carboplatin only:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended
Phenytoin: carboplatin reduces absorption and efficacy of phenytoin

References

- Summary of Product Characteristics Carboplatin (Hospira) accessed on 25 April 2024 via www.medicines.org.uk
- Summary of Product Characteristics Paclitaxel (Hospira) accessed on 25 April 2024 via www.medicines.org.uk
- Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment – supplementary appendix. *Lancet Oncol* 2019; **20:** e201–08.
- McCormack, M. et al. A Phase II study of weekly neoadjuvant chemotherapy followed by radical chemoradiation for locally advanced cervical cancer. Br J Cancer 2013;108:2464-2469
- McCormack, M. et al. A randomised phase II trial of induction chemotherapy followed by chemoradiation compared with chemoradiation alone in locally advanced cervical cancer: The GCIG INTERLACE trial. Annals of Oncology. 2023 34(suppl2);S1276.

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