Chemotherapy Protocol

GYNAECOLOGICAL CANCER

CARBOPLATIN (AUC5)-PACLITAXEL

(21 day)

Regimen

- Uterine-Carboplatin (AUC5)-Paclitaxel (21 day)

Indication

- Adjuvant treatment of high risk patients
- Metastatic endometrial cancer
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Carboplatin	Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances
Paclitaxel	Hypersensitivity, hypotension, bradycardia, peripheral neuropathy, myalgia and back pain on administration

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day each cycle
- EDTA or calculated creatinine clearance prior to each cycle
- CA125 prior to each cycle

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Prior to each cycle the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than $100x10^9$/L

Day 1

Neutrophils ($x10^9$/L)	Dose Modifications (carboplatin and paclitaxel)
1 or greater	100%
less than 1	Delay for 7 days. If the counts recover to at least $1x10^9$/L within this time continue with the full dose. If the counts do not recover within 7 days or repeated delays are required then delay until recovery then reduce the dose by 20%
Platelets ($x10^9$/L)	**Dose Modifications (carboplatin and paclitaxel)**
100 or greater	100%
50-99	Delay for 7 days. If the counts recover to at least $100x10^9$/L within this time then continue with the full dose. If counts do not recover within 7 days or repeated delays are required then delay until recovery then reduce dose by 20%
less than 50	Delay until recovery then reduce dose by 50%

Hepatic Impairment

Drug	Bilirubin (µmol/L)		AST/ALT units	Dose
Carboplatin	N/A		N/A	No dose adjustment needed
Paclitaxel	less than 21	and	less than 10xULN	175mg/m^2
	21-26			135mg/m^2
	27-51			75mg/m^2
	52-85			50mg/m^2
	greater than 85	or	greater than 10xULN	Contra indicated

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose
Carboplatin*	less than 20	Omit
Paclitaxel	N/A	No dose adjustment needed

* Significant changes in GFR of more than 10% may require dose adjustment.

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent should then be reduced to 75% of the original dose or discontinued as appropriate.

Regimen

The recommended maximum dose when using a calculated creatinine clearance at AUC5 is 750mg. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.

It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Carboplatin	AUC5	1	Intravenous infusion in 500ml glucose 5% over 60 minutes
Paclitaxel	175mg/m^2	1	Intravenous infusion in 500ml sodium chloride 0.9% over 180 minutes.

Dose Information

- The recommended maximum dose when using a calculated creatinine clearance at AUC5 is 750mg. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.
- It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.
- Carboplatin dose will be rounded to the nearest 50mg (up if halfway).
- Paclitaxel will be dose banded in accordance with the national dose bands (6mg/ml)

Administration Information

Extravasation

- Carboplatin – irritant
- Paclitaxel - vesicant

Other

- Hypersensitivity reactions tend to occur with the first or second infusion of paclitaxel. Paclitaxel infusion should be interrupted for minor symptoms such as flushing or localised rashes. If these resolve promptly (within 5 minutes) the infusion may be restarted at a lower rate with intensive monitoring. Immediately discontinue the infusion for severe reactions which include profound hypotension, bronchospasm and generalised erythema.
- Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter.

Additional Therapy

- Premedication to reduce of risk of hypersensitivity reaction

  30 minutes before chemotherapy

- chlorphenamine 10mg intravenous
- dexamethasone 20mg oral or intravenous
- H_2 antagonist according to local formulary choice and availability

- Antiemetics

  15-30 minutes prior to chemotherapy

  - ondansetron 8mg oral or intravenous

  As take home medication

  - dexamethasone 4mg oral twice a day for 3 days
  - metoclopramide 10mg oral three times a day as required

- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

References

1. Sehouli J, Runnebaum IB, Fotopoulou C et al. A randomised phase III adjuvant study in high risk cervical cancer: simultaneous radiochemotherapy with cisplatin (S-RC) versus systemic paclitaxel and carboplatin followed by percutaneous radiation (PC-R): a NOGGO-AGO Intergroup Study. Ann Oncol 2012; 23 (9): 2259-2264.
2. Hisamatsu T, Mabuchi S, Yoshino K et al. Prediction of progression free survival and response to paclitaxel plus carboplatin in patients with recurrent or advanced cervical cancer. Int J Gynecol Cancer 2012; 22 (4): 623-629.
3. Pectasides D, Fountzilas G, Papaxoinis G et al. Carboplatin and paclitaxel in metastatic or recurrent cervical cancer. Int J Gynecol Cancer 2009; 19 (4): 777-781.
4. NICE Guidance TA55 - Guidance on the use of paclitaxel in the treatment of ovarian cancer. Jan 2003
5. NICE Guidance TA91 - Ovarian cancer (advanced) - paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan (review). May 2005

REGIMEN SUMMARY

Carboplatin (AUC5)-Paclitaxel (21 day)

Day 1

1. Chlorphenamine 10mg intravenous

2. Dexamethasone 20mg intravenous

3. H_2 antagonist according to local formulary choice and availability
   Administration Instructions:
   Administer according to local formulary choice and availability one of the following 30 minutes prior to chemotherapy;
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only
   - ranitidine 50mg intravenous once only

   There are stock shortages of H_2 antagonists. The administration may proceed without these agents being given unless there is a specific instruction from the prescriber in the ARIA journal that a H_2 antagonist must be administered.
   Many Trusts do not administer an H_2 antagonist from cycle three onwards. They have been left in the ARIA protocols so that decisions can be made on an individual Trust and patient basis.

4. Ondansetron 8mg oral or intravenous

5. Paclitaxel 175mg/m^2 in 500ml sodium chloride 0.9% intravenous infusion over 180 minutes.
   Administration Instructions
   Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter.

6. Carboplatin AUC 5 intravenous infusion in 500ml glucose 5% over 60 minutes.

Take Home Medicines

7. Dexamethasone 4mg oral twice a day for 3 days starting the day after chemotherapy

8. Metoclopramide 10mg oral three times a day for three days then 10mg three times a day when required for nausea

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	October 2020	Update of premedication due to shortage of IV ranitidine. IV ranitidine changed to H_2 antagonist according to local formulary choice and availability Dose banding updated Coding removed	Arum Shortland Pharmacist	Dr Deborah Wright Pharmacist
1.2	March 2014	Carboplatin maximum dose added Bolus removed from "intravenous bolus" Dexamethasone dose in TTO clarified Disclaimer updated	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1.1	Dec 2013	Under regimen paragraph added regarding carboplatin dosing Metoclopramide dose changed Disclaimer added	Dr Deborah Wright Pharmacist	Liz Harrison Pharmacist
1	May 2013	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Clare Green Consultant Medical Oncologist Dr Cheng Yeoh Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.