Chemotherapy Protocol

GYNAECOLOGICAL CANCER

CARBOPLATIN Retreat

(AUC6)

Regimen

- Ovary – Carboplatin (AUC6) Retreat

Indication

- Second line or subsequent treatment of platinum sensitive ovarian cancer
- WHO performance status 0, 1

Toxicity

Drug	Adverse Effect
Carboplatin	Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances

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

Monitoring

- FBC, LFTs and U&Es 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

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

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

Day 1

Neutrophils ($x10^9$/L)	Dose Modifications
1 or greater	100%
less than 1	Delay for 7 days. If the counts recover to $1x10^9$/L or greater within this time continue with full dose. If the counts do not recover within 7 days or repeated delays are required then delay until recovery then reduce dose by 20%
Platelets ($x10^9$/L)	**Dose Modifications**
100 or greater	100%
50-99	Delay for 7 days. If the counts recover to $100x10^9$/L or greater within this time continue with 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 (% of original dose)
Carboplatin	N/A		N/A	No dose adjustment needed

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Carboplatin	less than 20	Omit

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 should then be reduced to 80% of the original dose or discontinued as appropriate.

Regimen

The starting dose of carboplatin AUC 6 is used with calculated GFR. AUC 5 may be considered with EDTA clearance, seek advice from the appropriate consultant before prescribing. The recommended maximum dose when using a calculated creatinine clearance at AUC6 is 900mg (creatinine clearance 125ml/min). This is not a dose included in the national dose banding table. The maximum dose has been set at 890mg in ARIA. Please check if this dose is appropriate. 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	AUC6 (max dose)	1	Intravenous infusion in 500ml glucose 5% over 60 minutes

Dose Information

- Carboplatin will be dose banded in accordance with the national dose bands (10mg/ml)
- The maximum dose of carboplatin for AUC6 is 900mg. This will be set as 890mg in ARIA to comply with national dose bands.
- 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.

Administration Information

Extravasation

- Carboplatin – irritant

Additional Therapy

- 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 for 3 days then as required

- Prevention of allergic reactions to carboplatin 30 minutes prior to chemotherapy

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

- 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. Paclitaxel plus carboplatin versus standard chemotherapy with either single agent carboplatin or cyclophosphamide doxorubicin, and cisplatin in women with ovarian cancer: the ICON3 randomised trial. Lancet 2002; 360:505-515.
2. ICON2: randomised trial of single agent carboplatin against three drug combination of CAP (cyclophosphamide, doxorubicin, and cisplatin) in women with ovarian cancer. ICON Collaborators. International Collaborative Ovarian Neoplasm Study. Lancet 1998;352(9140):1571-6.
3. Paclitaxel plus platinum based chemotherapy versus conventional platinum based chemotherapy in women with relapsed ovarian cancer: The ICON4/AGOOVAR2.2 trial. Lancet 2003; 361 (9375): 2099-2106.
4. Bolis G, Scarfone G, Giardina G, Villa A, Mangili G, Melpigano M, et al. Carboplatin alone vs carboplatin plus epidoxorubicin as second line chemotherapy for cisplatin or carboplatin sensitive ovarian cancer. Gynecol Oncol 2001;81:39.

REGIMEN SUMMARY

Carboplatin (AUC6) Retreat

Day One

1. Chlorphenamine 10mg intravenous

2. Dexamethasone 10mg oral or 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 SACT;
   - ranitidine 50mg intravenous once only
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only

   If there is no stock of these products due to national shortages treatment may proceed without the H_2 antagonist provided there is no instruction in the ARIA journal indication the patient **must have** H_2 antagonist treatment.

   All infusion related reactions must be recorded in the ARIA journal and reported to the appropriate consultant. 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
   Administration Instructions
   Administer as ondansetron 8mg intravenous if required

5. Carboplatin AUC 6 intravenous infusion in 500ml glucose 5% over 60 minutes.
   Administration Instructions
   The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 6 is 900mg. The national dose bands do not contain this dose so the cap has been set at 890mg in ARIA. Please check this dose is appropriate for your patient.

Take Home Medicines

6. Dexamethasone 4mg oral twice a day for 3 days starting on day 2 of the cycle
   Administration Instructions
   Take with or after food. Start on day two of the cycle.

7. Metoclopramide 10mg oral three times a day for three days then 10mg three times a day when required for nausea.
   Administration Instructions
   Please supply 28x10mg tablets or nearest equivalent pack size

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Aug 2022	Carboplatin changed to national dose bands Administration instructions added in summary	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1.1	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 Coding removed	Arum Shortland Pharmacist	Dr Deborah Wright Pharmacist
1	Sept 2014	None	Dr Deborah Wright Pharmacist	Dr V McFarlane Consultant Clinical 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 Hospital 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.