**Chemotherapy Protocol**

## GYNAECOLOGICAL CANCER

# CARBOPLATIN (AUC4)-GEMCITABINE (day 1)

## Regimen

- Ovary-Carboplatin (AUC4)-Gemcitabine (1)

## Indication

- Recurrent platinum sensitive ovarian cancer where re-treatment with paclitaxel is inappropriate
- WHO performance status 0, 1, 2

## Toxicity

| Drug | Adverse Effect |
|---|---|
| Carboplatin | Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances |
| Gemcitabine | Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza like symptoms, radiosensitising |

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 1 x$10^9$/L |
| Platelets | equal to or more than 100 x$10^9$/L |

**Day 1**

| Neutrophils (x$10^9$/L) | Dose Modifications (carboplatin and gemcitabine) |
|---|---|
| 1 or greater | 100% |
| less than 1 | Delay one week. If, at this point, the counts are 1x$10^9$/L or greater then continue with full dose. If the counts are still less than 1x$10^9$/L delay a further week and if the counts recover at this point continue with 80% dose of both agents. Otherwise consider stopping treatment. |
| **Platelets (x$10^9$/L)** | **Dose Modifications (carboplatin and gemcitabine)** |
| 100 or greater | 100% |
| 50-99 | Delay one week. If, at this point the platelets are 100x$10^9$/L or greater continue with full dose. If the platelets are still less than 100x$10^9$/L then delay a further week. If the counts recover at this point continue with 80% dose of both agents. Otherwise consider stopping treatment. |
| less than 50 | Delay until recovery to 100x$10^9$/L or greater then continue with 50% doses. |

### *Hepatic Impairment*

| Drug | Bilirubin µmol/L | | AST/ALT units | Dose |
|---|---|---|---|---|
| Carboplatin | N/A | | N/A | No dose adjustment needed |
| | | | | |
| Gemcitabine | 30 or greater | | N/A | Initiate treatment at 800mg/m$^2$ |

### *Renal Impairment*

| Drug | Creatinine Clearance (ml/min) | Dose (% of original dose) |
|---|---|---|
| Carboplatin* | less than 20 | Omit |
| | | |
| Gemcitabine | less than 30 | Consider dose reduction |

* 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 80% of the original dose or discontinued as appropriate.

## Regimen

The starting dose of carboplatin AUC 4 is used with calculated GFR. AUC 3 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 AUC 4 is 600mg (creatinine clearance 125ml/min). This is not a dose included in the national dose banding table. The maximum dose has been set at 630mg 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.

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 | AUC4 (max dose) | 1 | Intravenous infusion in 500ml Glucose 5% over 60 minutes |
| Gemcitabine | 1000mg/m$^2$ | 1 | Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes |

## Dose Information

- For elderly/frail patients or those with poor performance status consider using carboplatin AUC 3 and/or gemcitabine 750mg/m$^2$
- Carboplatin will be dose banded in accordance with the national dose bands (10mg/ml)
- The maximum dose of carboplatin for AUC 4 is 600mg. This will be set as 630mg 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.
- Gemcitabine will be dose banded in accordance with the national dose bands (100mg/ml).

## Administration Information

### *Extravasation*

- Carboplatin – irritant
- Gemcitabine - neutral

## Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy

  - dexamethasone 8mg oral or intravenous
  - 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.Pfisterer J, Plante M, Vergote I et al. Gemcitabine Plus Carboplatin Compared With Carboplatin in Patients With Platinum-Sensitive Recurrent Ovarian Cancer: An Intergroup Trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. J Clin. Oncol 2006; 24 (29): 4699-4707
2.Papadimitriou C, Fountzilas G, Aravantinos G et al. Second-line chemotherapy with gemcitabine and carboplatin in paclitaxel-pretreated, platinum-sensitive ovarian cancer patients: A Hellenic Cooperative Oncology Group Study. Gynecologic Oncology 2004; 92; 152-159

## REGIMEN SUMMARY

Carboplatin (AUC4)-Gemcitabine (1)

### Day 1

1. Dexamethasone 8mg oral or intravenous
   Administration Instructions
   May be given as 8mg intravenous if required.

2. Ondansetron 8mg oral or intravenous
   Administration Instructions
   May be given as 8mg intravenous if required

3. Gemcitabine 1000mg/$m^2$ in 250ml sodium chloride 0.9% intravenous infusion over 30 minutes.

4. Warning - Carboplatin Maximum Dose
   Administration Instructions
   The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 4 is 600mg. The national dose bands do not contain this dose so the cap has been set at 630mg in ARIA. Please check this dose is appropriate for your patient.

5. Carboplatin AUC 4 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 4 is 600mg. The national dose bands do not contain this dose so the cap has been set at 630mg 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 4mg twice a day (morning and lunch) for 3 days starting on day 2 of the cycle

7. Metoclopramide 10mg oral three times a day for three days and then 10mg three times a day when required for nausea
   Administration Instructions
   Please supply 28x10mg tablets or an original pack as appropriate

## DOCUMENT CONTROL

| Version | Date | Amendment | Written By | Approved By |
|---|---|---|---|---|
| 1.2 | Aug 2022 | Carboplatin changed to national dose bands<br>Warning added to summary<br>Instructions added to summary | Dr Deborah Wright<br>Pharmacist | Donna Kimber<br>Pharmacy Technician |
| 1.1 | April 2014 | Carboplatin maximum dose added<br>Bolus removed from intravenous bolus<br>Metoclopramide dose changed<br>OPCS code updated<br>Antiemetic start clarified<br>Disclaimer updated | Dr Deborah Wright<br>Pharmacist | Donna Kimber<br>Pharmacy Technician |
| 1 | May 2013 | None | Rebecca Wills<br>Pharmacist<br><br>Dr Deborah Wright<br>Pharmacist | Dr Clare Green<br>Consultant Medical Oncologist<br><br>Dr Cheng Yeoh<br>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 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.