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Gemcitabine + Carboplatin
Ovarian Cancer

**Background:** Patients with advanced ovarian cancer are generally best treated with combination therapy rather than single agents. Standard 1st line therapy is carboplatin + paclitaxel. If patients relapse after 12 months (platinum sensitive) they are normally retreated with the same regimen. However, some patients develop significant, permanent neurotoxicity from paclitaxel and are unable to receive this again. For this group a randomised trial has shown that gemcitabine plus carboplatin gives superior results to single agent carboplatin.

For patients who relapse between 6 and 12 months (partially platinum sensitive) further treatment with carboplatin + paclitaxel often leads to further response but this is generally transient (<6 months). Gemcitabine in place of paclitaxel offers another treatment option with less neuropathy and alopecia.

**Patient group:**

| Patients with recurrent ovarian cancer that have relapsed within 6-12 months after prior platinum therapy (single agent or combination).  
| Patients with recurrent ovarian cancer that have relapsed >12 months after platinum therapy, where paclitaxel is contraindicated.  
| ECOG PS 0-2 |

**Pre-treatment assessment:**
Weight, FBC, U&E’s, LFT’s and creatinine clearance (calculated)
CA125

**Treatment Threshold**
WBC > 3 x 10^9/L  
Platelets > 100 x 10^9/L  
ANC > 1.5 x 10^9/L
Administration:
- Hypersensitivity reactions to carboplatin may develop in patients who have been extensively pre-treated with carboplatin.

Pre-Meds: Chlorphenamine 10mg IV bolus and Hydrocortisone 100mg IV bolus administered 30 minutes prior to chemotherapy in patients who develop hypersensitivity to Carboplatin.

Anti-emetics: Highly emetic day 1 and Low on day 8

Additional Medication: None.

Monitoring and Assessment:
FBC—prior day 1 and day 8 of cycle
Clinical examination, U&E, LFTs and creatinine clearance (calculated)- prior to each cycle
CA125 – prior to each cycle
Radiology – to confirm response to treatment after 2nd or 3rd cycle

Dose Modifications:
The dose of carboplatin should remain the same throughout treatment. It should only be recalculated if the serum creatinine increases by ≥ 15% from baseline.

**Haematological Toxicity**

Day 1
If ANC < 1.5 x 10⁹/L and /or platelets < 100 x 10⁹/L, delay treatment by one week.
Reduce dose of gemcitabine to 800mg/m² and use Carboplatin AUC 4 if:
- ANC known to be less than 0.5 for greater than 5 days within a cycle

Regimen Details:

**Day 1**
- **Gemcitabine** 1000mg/m² IV in 250mL 0.9% sodium chloride infused over 30 minutes
- **Carboplatin** AUC 4/5* IV in 250-500ml Glucose 5% infused over 60 minutes.
  *Use AUC 4 in heavily pre-treated patients.

**Day 8**
- **Gemcitabine** 1000mg/m² IV in 250mL 0.9% sodium chloride infused over 30 minutes

**Cycles are repeated at intervals of 21 days for 6 cycles (max 10 cycles).**
• ANC known to be less than 0.1 for greater than 3 days within a cycle
• Febrile neutropenia occurred
• Platelets less than 50 within a cycle
• Cycle was delayed greater than 1 week due to toxicity

**Day 8**
If ANC < 1.0 x 10^9/L or platelets < 75 x 10^9/L omit gemcitabine and reduce dose of gemcitabine to 800mg/m^2 for subsequent cycles. If toxicity persists after dose reduction, omit Day 8 gemcitabine.

*Non-Haematological Toxicity*
For grade 3/4 non hematologic toxicities (except nausea/vomiting) dose reduction at clinician’s discretion.

**Hepatic Impairment**
If bilirubin > 27 µmol/L, reduce dose of gemcitabine to 800 mg/m^2

**Renal Impairment**
Gemcitabine: consider dose reduction if creatinine clearance < 30mL/min.
Carboplatin: As per Calvert formula.

**Pharmaceutical Care:**
- The creatinine clearance should be calculated using the Cockcroft & Gault Formula
  
  Females: \[
  1.04 \times (140 – \text{age}) \times \text{weight (kg)}
  \]
  
  Serum creatinine (micromol/l)

  Males: \[
  1.23 \times (140 – \text{age}) \times \text{weight (kg)}
  \]
  
  Serum creatinine (micromol/l)

- The dose of Carboplatin should be calculated using the Calvert Formula.
  
  Dose = AUC * (GFR + 25) mg

- A second pharmacist check is required for all calculations.

- Carboplatin may interact with aluminium to form a black precipitate. Needles, syringes, catheters or IV administration sets that contain aluminium parts which may come into contact with carboplatin, should not be used for the preparation or administration of the drug.

- Concurrent therapy with nephrotoxic or ototoxic drugs such as aminoglycosides, vancomycin, capreomycin and diuretics, may increase or exacerbate toxicity due to carboplatin induced changes in renal clearance.

- Yellow fever vaccine and other live attenuated vaccines are not recommended due to the risk of systemic, possibly fatal, disease, particularly in immunosuppressed patients.

**Most Common Toxicities:**
• Myelosuppression +/- infection
• Nausea and vomiting
• Rash
• Fatigue
• Constipation
• Diarrhoea
• Nephrotoxicity
• Neuropathy (mild)
• Ototoxicity
• Pulmonary Fibrosis (rare)
• ↑LFTs
• Haemolytic Uraemic Syndrome (rare)

References:

2. SPC Carboplatin Hospira UK Ltd [www.medicines.org.uk](http://www.medicines.org.uk) [accessed 3rd October 2012]