Carboplatin and Paclitaxel for Advanced, Metastatic or Recurrent Cervical / Endometrial / Vaginal Cancer

Indication:
1) Alternative first line to Cisplatin or second line in women with Advanced, Metastatic or Recurrent Cervical or Vaginal Cancer

2) Alternative first line to Doxorubicin / Cisplatin or second line in women with Advanced, Metastatic or Recurrent Endometrial Cancer

Regimen details:
- Paclitaxel 175mg/m² IV D1
- Carboplatin AUC 5 IV D1 (see Comments)

Administration: 
- Paclitaxel in 500mls Sodium Chloride 0.9% over 3 hours via non-PVC infusion bag, with a 0.22 micron in-line filter. Paclitaxel must be diluted to a concentration of 0.3-1.2mg/ml to maintain stability in clinical practice
- Carboplatin in 500mls Glucose 5% IV over 30-60 minutes

Any device containing aluminium that may come in contact with Carboplatin must be avoided

Premedication:
- Dexamethasone 20mg IV 30 – 60 minutes prior to Paclitaxel administration
- Chlorphenamine 10mg IV 30 – 60 minutes prior to Paclitaxel administration over at least 1 minute
- Ranitidine 50mg IV 30 – 60 minutes prior to Paclitaxel administration over at least 2 minutes

Frequency: Every 21 days, for a maximum of 6 cycles

Extravasation: Paclitaxel: Vesicant
Carboplatin: Non-vesicant

Anti-emetics: Moderate emetogenic
Follow local Anti-emetic Policy

Regular investigations:
- FBC D1
- U&Es D1
- LFTs D1
- CA–125 D1 (only for Endometrial Cancer)
- EDTA Prior to 1st cycle, if necessary (see Comments)
- CT scan (disease evaluation) After 3 cycles

Comments:
- Carboplatin dose should be calculated using the Calvert formula:
  \[ \text{Dose} = \text{Target AUC} \times (25 + \text{GFR}) \]
  GFR should be measured before the first cycle, by EDTA clearance or using the Cockcroft & Gault equation. Subsequent doses of Carboplatin should usually be based on this value of GFR.
  If the calculated GFR < 60 OR > 120ml/min, measure EDTA clearance or creatinine clearance before prescribing. Monitor trends in serum creatinine between treatments: if the patient’s serum Creatinine changes significantly (> 20% from baseline value), re-calculate GFR using the Cockcroft & Gault equation or measure EDTA clearance
DOSE MODIFICATIONS

Haematological Toxicity

Day 1

WBC < 3.0 x 10^9/ L or Neutrophils < 1.5 x 10^9/ L or Platelets < 100 x 10^9/ L

Delay for 1 week.
Repeat FBC - If within normal parameters, resume treatment with Carboplatin and Paclitaxel at 100% doses

Subsequent cycles

If Neutrophils < 0.5 x 10^9/ L for ≥ 7 days, OR Febrile neutropenia is diagnosed OR Platelets < 50 x 10^9/L for ≥ 7 days,

Dose reduce Paclitaxel to 135mg/m^2 and Carboplatin to AUC 4. If ongoing myelosuppression, despite the use of lower doses, discontinue therapy

Renal Impairment: Paclitaxel: No dose adjustment required. Assess renal function when clinically indicated
Carboplatin: Contraindicated if CrCl < 20ml/min

Hepatic Impairment: Paclitaxel is not recommended in severe impaired hepatic function:

<table>
<thead>
<tr>
<th>AST/ALT (units)</th>
<th>Paclitaxel Dose</th>
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</thead>
<tbody>
<tr>
<td>&lt; 2.5 x ULN</td>
<td>Give 100%</td>
</tr>
<tr>
<td>2.5 – 5 x ULN</td>
<td>Continue therapy at Consultant’s discretion</td>
</tr>
<tr>
<td>&gt; 5 x ULN</td>
<td>Discontinue therapy</td>
</tr>
</tbody>
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Carboplatin: No dose adjustment required

DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE

PERIPHERAL NEUROPATHY – PACLITAXEL

Grade | Neuropathy-sensory | Paclitaxel Dose
---|-------------------|-----------------|
1 | Paresthesia (including tingling) but not interfering with function | Give 175mg/m^2 |
2 | Paresthesia interfering with function, but not interfering with activities of daily living | Reduce Paclitaxel dose to 135mg/m^2 |
3 | Paresthesia interfering with activities of daily living | Discontinue therapy |
4 | Disabling | Discontinue therapy |
ARTHRALGIA / MYALGIA – PACLITAXEL

Paclitaxel may cause Grade 1 or 2 arthralgia or myalgia:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Arthralgia/Myalgia</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Joint and muscle pain, not interfering with function</td>
<td>Consider use of NSAIDs</td>
</tr>
<tr>
<td>2</td>
<td>Joint and muscle pain, interfering with function, but not interfering with activities of daily living</td>
<td>Consider use of NSAIDs</td>
</tr>
</tbody>
</table>

Toxicities: Myelosuppression; fatigue; nausea; vomiting; constipation; diarrhoea; mucositis; nephrotoxicity; neurotoxicity / ototoxicity; myalgia / arthralgia; taste disturbance; hypersensitivity reactions (mainly flushing, rash and hypotension); alopecia

Drug interactions:

Paclitaxel:
- Concomitant administration of inducers or inhibitors of cytochrome P450 Isoenzymes (CYP2C8 and 3A4) e.g. erythromycin, fluoxetine, gemfibrozil, rifampicin, carbamazepine, phenytoin, phenobarbital etc, may alter the pharmacokinetics of Paclitaxel, presenting a theoretical interaction

Carboplatin:
- Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
- Clozapine: increased risk of agranulocytosis, avoid concomitant use
- Diuretics: increased risk of nephrotoxicity and ototoxicity
- Neurotoxic drugs: increased nephrotoxicity; not recommended
- Phenytoin: reduced absorption of the antiepileptic
- Warfarin: increased anticoagulant effect of warfarin

References:
- www.medicines.org.uk
- UCLH-Dosage Adjustment for Cytotoxics in Hepatic Impairment. November 2003
- UCLH-Dosage Adjustment for Cytotoxics in Renal Impairment. November 2003
- GSTT Guidelines for treating Nausea and Vomiting in adult patients. September 2007
- CTCAE v3.0. August 2006