Paclitaxel and Carboplatin in Advanced Ovarian, Fallopian Tube and Primary Peritoneal Cancer

Indication: First or subsequent line Palliative therapy in women with Ovarian, Fallopian Tube and Primary Peritoneal Cancer who are Platinum-sensitive patients

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 6 cycles

Extravasation: Paclitaxel: Vesicant
Carboplatin: Non-vesicant

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

Regular investigations: FBC D1
LFTs D1
U&Es D1
CA 125 D1
Disease evaluation Every 3 cycles
EDTA Prior to 1st cycle, if necessary (see Comments)

Comments: Carboplatin dose should be calculated using the Calvert formula:
Dose= Target AUC x (25 + 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 10⁹/ L

or

Neutrophils < 1.5 x 10⁹/ L

or

Platelets < 100 x 10⁹/ L

Delay for 1 week.

or

Repeat FBC - If within normal parameters, resume treatment with Paclitaxel and Carboplatin at 100% doses

If Day 1 parameters are abnormal, as above, on more than one occasion, consider giving Paclitaxel 140mg/m² and Carboplatin AUC 4 doses

Subsequent cycles

If Neutrophils < 0.5 x 10⁹/ L for ≥ 7 days, OR
Febrile neutropenia is diagnosed OR
Platelets < 50 x 10⁹/ L,

Dose reduce both drugs to Paclitaxel 135mg/m² and Carboplatin AUC 4. If the patient continues to experience these side effects at the lower dose, give Paclitaxel 105mg/m² and Carboplatin AUC 3 or consider omitting Paclitaxel and continuing Carboplatin at full dose i.e AUC 5

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>Bilirubin (µmol/L)</th>
<th>Paclitaxel Dose (mg/m²)</th>
</tr>
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<tbody>
<tr>
<td>&lt; 26</td>
<td>135</td>
</tr>
<tr>
<td>27 – 51</td>
<td>75</td>
</tr>
<tr>
<td>&gt; 51</td>
<td>50</td>
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</tbody>
</table>

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/m² |
2      | Paresthesia interfering with function, but not interfering with activities of daily living | Reduce Paclitaxel dose to 135mg/m² |
3      | Paresthesia interfering with activities of daily living | Omit Paclitaxel |
4      | Disabling | Omit Paclitaxel |
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: anaemia; leukopenia; neutropenia; infection; thrombocytopenia; fatigue; nausea; vomiting; mucositis; diarrhoea; constipation; dysgeusia; hypersensitivity reactions (mainly flushing, rash and hypotension); peripheral neuropathy; alopecia; arthralgia; myalgia

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
- Nephrotoxic drugs: increased nephrotoxicity; not recommended
- Phenytoin: reduced absorption of the antiepileptic
- Warfarin: increased anticoagulant effect of warfarin

References:
www.medicines.org.uk
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CCO Formulary. PACLICARBO. Revised February 2007
SWSHCN- Network Approved Regimen for Ovarian Cancer. June 2008
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