Docetaxel and Carboplatin in NSCLC (Non-small cell lung cancer)

Indication: First line palliative therapy for previously untreated Stage IIIB or IV Non-small cell lung cancer patients

Regimen details:

<table>
<thead>
<tr>
<th>Docetaxel</th>
<th>Carboplatin</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>75mg/m²</td>
<td>AUC 6 (if C&amp;G)</td>
<td>Docetaxel in 250mls Sodium Chloride 0.9% IV over 1 hour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carboplatin in 500mls Glucose 5% IV over 30 – 60 minutes</td>
</tr>
</tbody>
</table>

OR

<table>
<thead>
<tr>
<th>Docetaxel</th>
<th>Carboplatin</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>75mg/m²</td>
<td>AUC 5 (if EDTA)</td>
<td>Docetaxel in 250mls Sodium Chloride 0.9% IV over 1 hour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carboplatin in 500mls Glucose 5% IV over 30 – 60 minutes</td>
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</tbody>
</table>

Premedication:

Dexamethasone 8mg po bd for 3 days, starting the morning of the day prior to each docetaxel administration, to reduce the incidence and severity of fluid retention and hypersensitivity reactions. If the patient has not taken the oral pre-med for any reason, Dexamethasone 20mg IV should be administered 1 hour prior chemotherapy

Frequency: 21 days, for 4 – 6 cycles

Extravasation:

Docetaxel: Vesicant
Carboplatin: Non-vesicant

Anti-emetics:

Docetaxel: Low emetogenic
Carboplatin: Moderate emetogenic

Regular investigation:

- FBC D1
- LFTs D1
- U&Es D1
- EDTA Prior to 1st cycle, if necessary (see Comments)
- CT scan Every 2 cycles

Comments:

DOCETAXEL: Hypersensitivity reactions may occur, during the first and second infusions, within a few minutes following the initiation of the infusion

Degree of symptoms

<table>
<thead>
<tr>
<th>Hypersensitivity reactions</th>
<th>Action</th>
</tr>
</thead>
</table>
| Minor                     | Flushing
| Localised cutaneous reaction | Do not require interruption of therapy. Administer prophylactic anti-anaphylactic medication before further cycles of Docetaxel |

Severe

<table>
<thead>
<tr>
<th>Severe</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe hypotension</td>
<td>Require immediate discontinuation of Docetaxel</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>Administer appropriate aggressive therapy</td>
</tr>
<tr>
<td>Generalised rash/erythema</td>
<td></td>
</tr>
</tbody>
</table>

CARBOPLATIN: The total dose should be calculated in milligrams, using the Calvert formula
Dose = Target AUC x (25 + GFR)
GFR should be calculated using the Cockcroft & Gault equation in all patients; if the calculated GFR < 60 or > 120ml/min, measure EDTA clearance or creatinine clearance before prescribing. Carboplatin dose is calculated as AUC 5 if EDTA is used. Monitor trends in serum creatinine between treatments: if 25% from baseline value, re-calculate GFR using the Cockcroft & Gault equation.

**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 
100% doses

Subsequent cycles

If Neutrophils < 0.5 x 10\(^9\)/L for 1 week, OR 
Febrile neutropenia is diagnosed, OR 
Platelets < 25 x 10\(^9\)/L, 
Docetaxel dose should be reduced to 60mg/m\(^2\) and Carboplatin dose should be reduced by 1 x AUC, from previous doses, respectively (do not escalate for subsequent cycles). If the patient continues to experience these side effects at the lower dose, treatment should be discontinued.

**Renal Impairment**

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

**Hepatic Impairment**

Carboplatin: No dose adjustment required
Docetaxel: The dose should be adjusted as follows:

<table>
<thead>
<tr>
<th>ALP and AST/ALT</th>
<th>Biliirubin</th>
<th>Docetaxel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2.5 x ULN</td>
<td>≤ 1.5 x ULN</td>
<td>Full dose</td>
</tr>
<tr>
<td>2.6 - 6 x ULN</td>
<td>1.6 - 3.5 x ULN</td>
<td>75% dose</td>
</tr>
<tr>
<td>&gt; 6 xULN</td>
<td>&gt; 3.5 x ULN</td>
<td>And/or &gt; 22µmol/l</td>
</tr>
</tbody>
</table>

**DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Cutaneous reactions</th>
<th>Neuropathy-sensory</th>
<th>Docetaxel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Erythema without associated symptoms</td>
<td>Paresthesia (including tingling) but not interfering with function</td>
<td>100% dose</td>
</tr>
<tr>
<td>2</td>
<td>Localized erythema of the palms of the hands and soles of the feet with oedema followed by desquamation</td>
<td>Paresthesia interfering with function, but not interfering with ADL</td>
<td>May consider dose reduction: Docetaxel 60mg/m(^2)</td>
</tr>
<tr>
<td>3</td>
<td>Severe, generalised eruptions followed by desquamation</td>
<td>Paresthesia interfering with ADL</td>
<td>Delay Docetaxel until recovery to Grade ≤ 2, thereafter, reduce dose to Docetaxel 60mg/m(^2)</td>
</tr>
<tr>
<td>4</td>
<td>Generalised exfoliative, ulcerative, or bullous dermatitis</td>
<td>Disabling</td>
<td>Discontinue Docetaxel permanently</td>
</tr>
</tbody>
</table>

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Reason for Update: Network Protocol Development

Version: 1  
Approved by Lung Consultant: James Spicer

Supersedes: All other versions  
Date: 01-09-08

Prepared by: Maria Teresa Pacheca-Palomar July’08  
Checked by (Network Pharmacist): J. Turner

Approved by SELCN DTAC Chair: Nic Ketley  
Date: Sept 08

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Toxicities: Myelosuppression; anaemia; asthenia; alopecia; nausea; vomiting; hypersensitivity reactions; cutaneous reactions; peripheral neuropathy; fluid retention; diarrhoea; stomatitis; ovarian failure; infertility

Drug interactions: Docetaxel:
- Concomitant administration of substrates, inducers or inhibitors of cytochrome P450-3A e.g. ciclosporin, terfenadine, ketoconazole, erythromycin etc, may alter the pharmacokinetics of Docetaxel, 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

References:
www.medicines.org.uk
Fosella et al. J Clin Oncol 21(16);3016-3024, 2003
GSTT guidelines for treating nausea and vomiting in adult patients. September 2007
UCLH- Dosage Adjustment for Cytotoxics in Renal Impairment. November 2003
UCLH- Dosage Adjustment for Cytotoxics in Hepatic Impairment. November 2003
CTCAE v3.0. August 2006