Lung Pathway Group – Docetaxel in Non-Small Cell Lung Cancer (NSCLC)

Indication: Second-line palliative therapy for advanced or metastatic NSCLC after failure of platinum chemotherapy

Regimen details: Docetaxel 60 - 75 mg/m² IV Day 1

Administration: Docetaxel in 250ml or 500ml Sodium Chloride 0.9% depending on final concentration IV over 1 hour

Hypersensitivity reactions may occur, such as flushing, rash with or without pruritus, chest tightness, back pain, dyspnoea and fever or chills, usually during the first and second infusions and within a few minutes following the start of the infusion; the infusion should be slowed down or interrupted and the necessary supportive medication should be administered. Severe reactions such as hypotension and/or bronchospasm or generalised rash/erythema requires immediate discontinuation. Availability of resuscitation equipment must be ensured as a standard precaution.

Frequency: Day 1, every 21 days, for 6 cycles

Pre-medication: Oral dexamethasone 8mg BD for 3 days, starting the day before docetaxel administration to reduce the incidence and severity of fluid retention and hypersensitivity reactions. If the patient has not taken the oral premedication, clinicians may prescribe dexamethasone IV 20mg, chlorphenamine IV 10mg and ranitidine IV 50mg to be administered 1 hour prior to chemotherapy. (Note: there is no data available to support the use of IV steroids in this setting, responsibility remains with the prescribing clinician).

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Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever.

Anti-emetics: Low emetogenicity
Follow Local Anti-emetic Policy

Supportive medication: Mouthcare as per local policy

Extravasation: Vesciant
Docetaxel should be administered with appropriate precautions to prevent extravasation.
If there is any possibility that extravasation has occurred, contact a senior member of the medical team and follow local protocol for dealing with cytotoxic extravasation

Regular investigations:
Prior to cycle 1
- FBC Day 1 (within 14 days)
- LFTs Day 1 (within 14 days)
- U&Es Day 1 (within 14 days)
- CT scan Baseline

Prior to Day 1 (all cycles)
- FBC Day 1 (within 72 hours)
- LFTs Day 1 (within 72 hours)
- U&Es Day 1 (within 72 hours)
- Imaging After 3 cycles

Toxicities: Neutropenia (reversible), anaemia, nausea, vomiting, diarrhoea, stomatitis, asthenia, peripheral neuropathy, hypersensitivity reactions, fluid retention, cutaneous reactions, alopecia, nail disorder, cystoid macular oedema, ovarian failure, infertility.

DOSE MODIFICATIONS

Haematological Toxicity

<table>
<thead>
<tr>
<th>Neutrophils (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.5 &amp; ≥ 100</td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>&lt; 1.5 or &lt; 100</td>
<td></td>
<td>Delay for 1 week. Repeat FBC, if recovered to above these levels, resume at 100% dose. Consider dose reduction for &gt;1 delay.</td>
</tr>
</tbody>
</table>

Version: 1.0 Supersedes: all other versions
Approved by LCA Lung Pathway Chemotherapy Lead: Dr Rohit Lal

Reason for Update: LCA Protocol Development
Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl

Prepared by: Lisa Yuen
Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson

Second check by: Laura Cameron
Date prepared: November 2014
Review Date: November 2016

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Reduce dose to 60 mg/m² if:
Neutrophils < 0.5 x 10⁹/L for more than 1 week,
Or febrile neutropenia diagnosed,
Or platelets < 50 x 10⁹/L
Do not escalate for subsequent cycles.

Non-haematological Toxicities

Renal Impairment
No dose adjustment required.

Hepatic Impairment

<table>
<thead>
<tr>
<th>ALP</th>
<th>AST / ALT</th>
<th>Bilirubin</th>
<th>Docetaxel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2.5 X ULN &amp; ≤ 1.5 x ULN</td>
<td>100% dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5 – 6 x ULN &amp; 1.6 – 3.5 x ULN</td>
<td>75% dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 6 ULN &amp; &gt; 3.5 x ULN &amp; / or &gt; 22µmol/L</td>
<td>Not recommended. Docetaxel should be administered with Consultant approval</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dose modifications for other toxicities as appropriate

<table>
<thead>
<tr>
<th>NCI CTCAE Grade</th>
<th>Cutaneous Reactions</th>
<th>Docetaxel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Erythema without associated symptoms</td>
<td>100% dose</td>
</tr>
<tr>
<td>2</td>
<td>Localised erythema of the palms of the hands and soles of the feet with oedema followed by desquamation</td>
<td>Consider dose reduction to 75% dose</td>
</tr>
<tr>
<td>3</td>
<td>Severe, generalised eruptions followed by desquamation</td>
<td>Delay until recovery to ≤ Grade 2, reduce to 75% dose For 2nd occurrence, discontinue docetaxel</td>
</tr>
<tr>
<td>4</td>
<td>Generalised exfoliative, ulcerative or bullous dermatitis</td>
<td>Discontinue docetaxel permanently</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>NCI CTCAE Grade</th>
<th>Sensory Neuropathy</th>
<th>Docetaxel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Paraesthesia (including tingling), but not interfering with function</td>
<td>100% dose</td>
</tr>
<tr>
<td>2</td>
<td>Paraesthesia interfering with function, but not interfering with activities of daily living</td>
<td>Consider dose reduction to 75% dose</td>
</tr>
<tr>
<td>3</td>
<td>Paraesthesia interfering with activities of daily living</td>
<td>Delay until recovery to ≤ Grade 2, reduce to 75% dose</td>
</tr>
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<tr>
<th>Location of regimen delivery:</th>
<th>Outpatient setting</th>
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<tr>
<td></td>
<td>Availability of resuscitation equipment must be ensured as a standard precaution.</td>
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**Drug interactions:**

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 potential interaction.

**References:**

Shepherd F.A. et al, J Clin Oncol (2000), Vol 18 (10); 2095 – 2103