Docetaxel & Prednisolone for Metastatic Castration Refractory Prostate Cancer

Indication: Palliative therapy in Metastatic Castration Refractory Prostate Cancer

Regimen details: Docetaxel 75mg/m² IV D1  
Prednisolone 10mg PO D1 – D21

Administration: Docetaxel in 250mls Sodium Chloride 0.9% as an IV infusion over one hour (PVC-free)

Prednisolone should be given orally once daily, in the morning, with or after food. Available as 5mg tablets. Use plain tablets only

Premedication: Oral Dexamethasone 8 mg; 12 hours, 3 hours and 1 hour before Docetaxel infusion, to reduce the incidence and severity of fluid retention and hypersensitivity reactions (see Comments). If the patient has not taken the oral pre-med for any reason, Dexamethasone 20mg IV should be administered 1 hour prior to chemotherapy

Frequency: Docetaxel - Every 21 days until disease progression for a maximum of 10 cycles  
Prednisolone - Continuous throughout chemotherapy

Extravasation: Docetaxel: Vescicant

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

Supportive medication: Growth factor support may be considered in patients with complicated neutropenia in subsequent cycles

Use of Proton Pump Inhibitor may be considered for ulcers caused by prolonged use of Prednisolone

Other medication: Androgen ablative therapy should be maintained throughout course of chemotherapy

Regular investigations:  
FBC Day 1  
LFTs Day 1  
U&Es Day 1  
PSA Every cycle  
Clinical Toxicity Assessment Every cycle

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 or until completely recovered

Repeat FBC – If within normal parameters, resume treatment with 100% Docetaxel dose

Reduce dose if subsequent cycles are also delayed (see below)

Subsequent cycles

| Reason for Update: Network Protocol Development | Approved by Urology Consultant: Hartmut Kristeleit |
| Supersedes: All other versions | Date: 10.02.10 |
| Prepared by: M.Teresa Pacheca-Palomar | Checked by (Network Pharmacist): Jacky Turner |
| Approved by SELCN DTAC Chair: Nic Ketley | Date: 24/02/2010 |
Docetaxel dose should be reduced to 60mg/m² if:

- Neutrophils < 0.5 x 10⁹/L for more than 1 week, OR
- Febrile neutropenia is diagnosed, OR
- Platelets < 50 x 10⁹/L

Do not escalate for subsequent cycles. If the patient continues to experience these side effects at the lower dose, treatment should be discontinued.

### Hepatic Impairment

<table>
<thead>
<tr>
<th>ALP and AST/ALT and/or Bilirubin</th>
<th>Docetaxel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 6 x ULN and ≤ 3.5 x ULN</td>
<td>Give full dose</td>
</tr>
<tr>
<td>&gt; 6 x ULN and &gt; 3.5 x ULN</td>
<td>Not recommended. Docetaxel should be administered with Consultant approval</td>
</tr>
<tr>
<td>&gt; 22µmol/L</td>
<td></td>
</tr>
</tbody>
</table>

Docetaxel clearance is reduced in patients with abnormal liver function, and an increased incidence of adverse effects (including treatment-related mortality) has been reported in patients with moderate to severe hepatic impairment.

### Renal Impairment

No dose adjustment required. Assess renal function when clinically indicated.

DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE

CUTANEOUS REACTIONS / PERIPHERAL NEUROPATHY - DOCETAXEL

<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 (75mg/m²)</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 activities of daily living</td>
<td>Consider reducing Docetaxel dose to 60mg/m²</td>
</tr>
<tr>
<td>3</td>
<td>Severe, generalised eruptions followed by desquamation</td>
<td>Paresthesia interfering with activities of daily living</td>
<td>Delay Docetaxel until recovery to grade ≤ 2, thereafter, reduce Docetaxel dose to 60mg/m². If symptoms persist, discontinue Docetaxel</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>
Toxicities: Neutropenia; leucopenia; thrombocytopenia; anaemia; alopecia; nausea; vomiting; stomatitis; diarrhoea; asthenia; peripheral neuropathy; hypersensitivity reactions; fluid retention; cutaneous reactions (reversible); alopecia; nail disorder; peptic ulceration

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.
Docetaxel may affect the pharmacokinetics of epirubicin and doxorubicin

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

Degree of symptoms | Hypersensitivity reactions | Action
--- | --- | ---
Minor | Flushing | Do not require interruption of therapy
Localised cutaneous reaction | Administer prophylactic anti-anaphylactic medication before further cycles of Docetaxel
Severe | Severe hypotension / Bronchospasm / Generalised rash / erythema | Require immediate discontinuation of Docetaxel
Administer appropriate aggressive therapy
Do NOT rechallenge

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GSTT guidelines for treating nausea and vomiting in adult patients. September 2007
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