Mitoxantrone & Prednisolone for Metastatic Castration Refractory Prostate Cancer

Indication: Alternative Palliative therapy to Docetaxel in patients with Metastatic Castration Refractory Prostate Cancer of less good performance status according to physician’s discretion

Regimen details: Mitoxantrone 12mg/m² IV D1
Prednisolone 10mg OD PO D1 – D21

Administration: **Mitoxantrone** IV diluted to at least 50 ml of Sodium Chloride 0.9% infusion over 15 – 30 minutes. Mitoxantrone should not be mixed with other drugs in the same infusion
**Prednisolone** should be given orally once daily, with or after food. Available as 5mg tablets. Use plain tablets only

Frequency: Mitoxantrone - Every 21 days, for 6 cycles.
Prednisolone - Continuous throughout chemotherapy

Extravasation: Mitoxantrone: Non - vesicant

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

Supportive medication: Use of Proton Pump Inhibitor may be considered for the prevention of ulcers caused by prolonged use of Prednisolone.

Regular investigations: FBC D1, (D10-14 of cycle 1)
LFTs D1
U&Es D1
PSA D1
Clinical Toxicity Assessment Every cycle
MUGA scan/Echocardiogram If clinically indicated (See Comments)

Comments: Maximum cumulative dose Mitoxantrone= 160mg/m²
A baseline MUGA scan should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy. MUGA scan should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum.

DOSE MODIFICATIONS:

Haematological

**D1**

WBC < 3.0 x 10⁹/L
or
Neutrophils < 1.5 x 10⁹/L
or
Platelets < 100 x 10⁹/L

Delay for 1 week or until completely recovered
Repeat FBC – If within normal parameters, resume treatment with
100% Mitoxantrone dose

<table>
<thead>
<tr>
<th>Reason for Update: Network Protocol Development</th>
<th>Approved by Urology Consultant: Hartmut Kristeleit</th>
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<tbody>
<tr>
<td>Version: 1</td>
<td>Supersedes: All other versions</td>
</tr>
<tr>
<td>Prepared by: Maria Teresa Pacheca Palomar Feb’10</td>
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<td>Approved by SELCN DTAC Chair: Nic Ketley</td>
<td>Date: 30.03.10</td>
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<tr>
<td>Approved by SELCN DTAC Chair: Nic Ketley</td>
<td>Date: 26.04.10</td>
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Subsequent cycles

Dose reduction of Mitoxantrone in subsequent cycles depend on nadir FBC on day 10-14 of cycle 1:

<table>
<thead>
<tr>
<th>Neutrophils</th>
<th>Platelets</th>
<th>Mitoxantrone Dose</th>
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</thead>
<tbody>
<tr>
<td>≥ 0.5 x 10⁹/L</td>
<td>≥ 50 x 10⁹/L</td>
<td>Give 12mg/m² on subsequent cycles</td>
</tr>
<tr>
<td>&lt; 0.5 x 10⁹/L or &lt; 50 x 10⁹/L</td>
<td></td>
<td>Give 10mg/m² on subsequent cycles</td>
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Renal Impairment
No dose adjustment required

Hepatic Impairment
Careful supervision is recommended when treating patients with severe hepatic insufficiency:

<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>Performance status</th>
<th>Mitoxantrone Dose</th>
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<tbody>
<tr>
<td>&lt; 59</td>
<td>Good</td>
<td>Give 100%</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>Good</td>
<td>Give 60%</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>Poor</td>
<td>Not recommended</td>
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</tbody>
</table>

DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE

NON – HAEMATOLOGICAL TOXICITY

For any Grade 3 – 4 toxicity, treatment should be deferred until recovery, and then continued with an appropriate dose reduction. Discuss with Consultant

Toxicities:
- Myelosuppression;
- anaemia;
- infection;
- nausea;
- vomiting;
- diarrhoea;
- constipation;
- stomatitis;
- abdominal pain;
- alopecia;
- cardiotoxicity;
- urine discolouration

Drug interactions:
- Mitoxantrone
  - Cardiotoxic drugs: increase the risk of cardiac toxicity
  - Immunosuppressive chemotherapy: use with caution

References:
- www.medicines.org.uk
- Summary of Product Characteristics Deltacortril. Alliance Pharmaceuticals Feb 2009
- SWSHCN – Network Approved Regimen Mitoxantrone and Prednisolone. Dec’07
- GSTT guidelines for treating nausea and vomiting in adult patients. September 2007
- NLCN - Dosage Adjustment for Cytotoxics in Renal Impairment. November 2003
- NLCN - Dosage Adjustment for Cytotoxics in Hepatic Impairment. November 2003