Paclitaxel in Adjuvant Breast Cancer

Indication: Adjuvant alternative therapy to Docetaxel, for high risk patients unable to tolerate Docetaxel

Regimen details:

Paclitaxel 175mg/m² IV D1 (q21 days)
OR
Paclitaxel 80mg/m² IV D1 (q7 days)

Administration:

Paclitaxel in 500mls Sodium Chloride 0.9% over 3 hours (if given 3-weekly)
OR
Paclitaxel in 250mls Sodium Chloride 0.9% over 1 hour (if given weekly)

Paclitaxel to be given 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.

Premedication:

Dexamethasone 20mg IV 30 – 60 minutes prior to paclitaxel administration (3-weekly)
OR
Dexamethasone 8mg IV 30 – 60 minutes prior to paclitaxel administration (weekly)

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 4 cycles
OR
Every 7 days, for 12 cycles

Extravasation: Paclitaxel: Vesicant

Anti- emetics: Paclitaxel: Low emetogenic. Follow local Anti-emetic policy

Regular investigations:

FBC D1
LFTs D1
U&Es D1

Dose Modifications

Haematological Toxicity

Day 1

WBC < 3.0 x 10⁹/l
or
Neutrophils < 1.0 x 10⁹/l
or
Platelets < 100 x 10⁹/l

Delay for 1 week.
Repeat FBC - If within normal parameters, resume treatment with 100% Paclitaxel dose.

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In adjuvant treatment, dose reduction and delays can compromise outcome. G-CSF should be considered if more than one delay and/ or before dose reduction. If in doubt, contact the relevant Consultant

**Subsequent cycles**

If Neutrophils < 0.5 x 10^9/ L for ≥ 7 days, OR
Febrile neutropenia is diagnosed OR
Platelets < 50 x 10^9/ L,
Seek Consultant advice and consider a longer course of G-CSF or a dose reduction to 80% from previous Paclitaxel dose (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**  No dose adjustment required. Assess renal function when clinically indicated

**Hepatic Impairment**  Patients with severe hepatic impairment should not be treated with Paclitaxel:

<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>Paclitaxel Dose (mg/m²)</th>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>

**DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE**

**PERIPHERAL NEUROPATHY – PACLITAXEL**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Neuropathy-sensory</th>
<th>Paclitaxel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Paresthesia (including tingling) but not interfering with function</td>
<td>Give 175mg/m²</td>
</tr>
<tr>
<td>2</td>
<td>Paresthesia interfering with function, but not interfering with activities of daily living</td>
<td>Reduce Paclitaxel dose to 135mg/m²</td>
</tr>
<tr>
<td>3</td>
<td>Paresthesia interfering with activities of daily living</td>
<td>Omit Paclitaxel</td>
</tr>
<tr>
<td>4</td>
<td>Disabling</td>
<td>Omit Paclitaxel</td>
</tr>
</tbody>
</table>

**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; neutropenia; thrombocytopenia; fatigue; nausea; vomiting; mucositis; diarrhoea; dysgeusia; hypersensitivity reactions (mainly flushing, rash and hypotension); infection; peripheral neuropathy; arthralgia; myalgia; alopecia

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
- Clozapine: avoid concomitant use, increased risk of agranulocytosis

References:
www.medicines.org.uk
Simpson D. et al. ISSN 2004, Vol 64 (16):1839-1849
Ring A E et al. Cancer Treatment Reviews (2005); 31:618-627
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