Paclitaxel, weekly, (+/- Trastuzumab or Bevacizumab) in Metastatic Breast Cancer

Indication:

**Single agent**
An alternative to three weekly schedules of taxanes in frail patients or bone marrow involvement or impaired liver function

**With Trastuzumab**
First line palliative therapy, with or without Trastuzumab, for Metastatic Breast Cancer patients who over-express HER-2 at a 3+ level and for whom an anthracycline is not suitable

**With Bevacizumab**
First line treatment of metastatic breast carcinoma with either Triple-negative tumour and/ or post prior taxane therapy.

LCNDG criteria to be met:
- Histologically or cytologically confirmed metastatic breast cancer
- No previous systemic chemotherapy for metastatic disease (except hormones)
- ER, PR and HER2 negative and/or previously treated with taxane in the adjuvant setting, with a disease free interval of at least 12 months after completion of taxane therapy
- ECOG performance status less than or equal to 1

Regimen details: For details of doses, monitoring and ongoing treatment, see separate protocol for Trastuzumab or Bevacizumab

**Single agent**
Paclitaxel 80mg/m² (*) IV D1 (without Trastuzumab)

**With Trastuzumab**
Paclitaxel 80mg/m² (*) IV D2 of the 1st cycle, then every 7 days on the same day as Trastuzumab

(*) Consultant may consider Paclitaxel 70 – 100mg/m², depending on patient status

**With Bevacizumab**
Paclitaxel 90mg/m² IV D1, D8 and D15 (every 28 days)
(Bevacizumab given on D1 and D15)

Administration:
Paclitaxel in 250mls Sodium Chloride 0.9% over 1 hour 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

When used in combination with Trastuzumab, Paclitaxel infusion may be started the day following the first dose of Trastuzumab or immediately after the subsequent doses of Trastuzumab if the preceding dose of Trastuzumab was well tolerated

Premedication:
- Dexamethasone 8mg IV 30 – 60 minutes prior to paclitaxel administration
- 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:

**Single agent or with Trastuzumab**  Cycle is 7 days, for up to 18 cycles

**With Bevacizumab**  Cycle is 28 days. Up to 6 cycles (18 doses) of Paclitaxel may be given.

Extravasation:  Paclitaxel: Vesicant

Anti- emetics:  Paclitaxel: Low emetogenic

Follow Local Anti-emetic Policy

Regular investigations:

- FBC  Prior each dose
- LFTs  3-4 weekly (D1 of 28/7 cycle)
- U&Es  3-4 weekly (D1 of 28/7 cycle)
- CT scan  Every 9 to 12 weeks routinely

** Blood cell counts should be obtained at least 24 hours prior to chemotherapy administration date

DOSE MODIFICATIONS

**Haematological Toxicity Day 1**

**Single agent or with Trastuzumab**

- WBC < 3.0 x 10^9/l  Delay for 1 week.
  - or  Repeat FBC - If within normal parameters, resume treatment with 100% Paclitaxel dose
- Neutrophils < 1.5 x 10^9/l  or
- Platelets < 50 x 10^9/l*

**With Bevacizumab**

- WBC < 3.0 x 10^9/l  Delay for 1 week.
  - or  Repeat FBC - If within normal parameters, resume treatment with 100% Paclitaxel dose
- Neutrophils < 1.5 x 10^9/l  or
- Platelets < 100 x 10^9/l*

**Subsequent cycles**

If Neutrophils < 0.5 x 10^9/L for ≥ 7 days, OR
Febrile neutropenia is diagnosed OR
Platelets < 25 x 10^9/L, Paclitaxel dose should be permanently reduced to 80% (or to 65mg/m² when given with Bevacizumab) for subsequent cycles
Renal Impairment: No dose adjustment required. Assess renal function when clinically indicated.

Hepatic Impairment: Paclitaxel is not recommended in severe impaired hepatic function.

<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>Paclitaxel Dose (mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 – 26</td>
<td>Give 75 – 80%</td>
</tr>
<tr>
<td>27 – 51</td>
<td>Give 40 – 45%</td>
</tr>
<tr>
<td>&gt; 51</td>
<td>Give 30%</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)</td>
<td>Give 100% dose</td>
</tr>
<tr>
<td></td>
<td>but not interfering with function</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Paresthesia interfering with function,</td>
<td>Give 80% dose</td>
</tr>
<tr>
<td></td>
<td>but not interfering with activities of daily living</td>
<td></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, cardiac changes.
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, accessed April 2012
www.micromedex.com, accessed April 2012
CDF SELCN documentation, April 2012
Seidman AD et al. JCO (2008); 26 (10): 1642 - 1649