Breast Pathway Group – Paclitaxel weekly in Advanced Breast Cancer

Indication: Advanced breast cancer, where initial chemotherapy (including an anthracycline) has failed or is inappropriate. The weekly regimen can be considered as an alternative in frail patients or for patients with bone marrow involvement or impaired liver function.

Regimen details: Paclitaxel *70 - 90mg/m² IV Day 1
* Consultant to decide dose basis, depending on patient status

If given with trastuzumab, for cycle 1 only, give trastuzumab on Day 1 and paclitaxel on day 2. For subsequent cycles, administer the trastuzumab followed by the paclitaxel. For details of doses, monitoring and on-going treatment with trastuzumab, see separate protocol for trastuzumab in the advanced setting.

Administration: Paclitaxel in 250ml Sodium Chloride 0.9% or Glucose 5% over 60 minutes. 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.

Frequency: Day 1, every 7 days, for 18 cycles

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
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*To minimise steroid side effects, the dose of dexamethasone may be reduced to 4mg if there has been no evidence of hypersensitivity

Paraceramol / 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: Vesicant
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 to reduce the risk of permanent tissue damage

Regular investigation:

Prior to Cycle 1:
- FBC Day 1 (within 14 days)
- LFTs Day 1 (within 14 days)
- U&Es Day 1 (within 14 days)

Prior to Day 1 (all cycles):
- FBC Day 1 (within 48 hours)

Prior to Day 1, Cycles 4, 7, 10, 13, 16
- LFTs Day 1 (within 48 hours)
- U&Es Day 1 (within 48 hours)

CT scan Every 9 to 12 weeks

Toxicities:
Anaemia, neutropenia, thrombocytopenia, fatigue, nausea, vomiting, mucositis, diarrhoea, dysgeusia, hypersensitivity reactions (mainly flushing, rash and hypotension), infection, peripheral neuropathy, arthralgia, myalgia, alopecia
DOSE MODIFICATIONS

Haematological Toxicity

<table>
<thead>
<tr>
<th>Neutrophils (x $10^9$/L)</th>
<th>Platelets (x $10^9$/L)</th>
<th>Paclitaxel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.5</td>
<td>≥ 50</td>
<td>100%</td>
</tr>
<tr>
<td>&lt; 1.5</td>
<td>&lt; 50</td>
<td>Delay for 1 week. Repeat FBC - if recovered to above these levels resume treatment with 100% dose</td>
</tr>
</tbody>
</table>

If neutrophils < 0.5 x $10^9$/L for ≥ 7 days, OR Febrile neutropenia is diagnosed OR Platelets < 25x $10^9$/L, Paclitaxel dose should be permanently reduced to 80% for subsequent cycles.

Non-haematological Toxicities

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

Hepatic Impairment

<table>
<thead>
<tr>
<th>Bilirubin (μmol/L)</th>
<th>Paclitaxel Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 - 26</td>
<td>Give 75 – 80% dose</td>
</tr>
<tr>
<td>27 – 51</td>
<td>Give 40 – 45% dose</td>
</tr>
<tr>
<td>&gt; 51</td>
<td>Give 30% dose</td>
</tr>
</tbody>
</table>

Dose modifications for other toxicities

PERIPHERAL NEUROPATHY

<table>
<thead>
<tr>
<th>NCI CTCAE Grade</th>
<th>Sensory Neuropathy</th>
<th>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>80% dose</td>
</tr>
<tr>
<td>3</td>
<td>Paraesthesia interfering with activities of daily living</td>
<td>Omit paclitaxel</td>
</tr>
<tr>
<td>4</td>
<td>Disabling</td>
<td>Discontinue paclitaxel permanently</td>
</tr>
</tbody>
</table>

Disclaimer: The Breast Pathway Group – Paclitaxel weekly in Advanced Breast Cancer is a sub-group of the LCA (London Cancer Alliance) Integrated Cancer System (ICS). The output of the ICS is documentation that can be adopted by healthcare organisations at their discretion. It is the responsibility of each individual organisation to ensure that appropriate governance and safety clearance procedures within their own clinical service have been followed prior to implementation of any such pieces of work. LCA assume no responsibility for this process within individual organisations, and no responsibility for the clinical management of individual patients or patient groups. Any clinical queries regarding individual patients or documentation should be directed to the relevant clinical team within the most appropriate healthcare organisation.

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ARTHRALGIA / MYALGIA
Paclitaxel may cause Grade 1 or 2 Arthralgia or myalgia

<table>
<thead>
<tr>
<th>NCI CTCAE 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>

Location of regimen delivery: Out-patient setting
Availability of resuscitation equipment must be ensured as a standard precaution

Comments: None

Drug interactions:
Concomitant administration of inducers or inhibitors of cytochrome P450 Isoenzymes (CYP2C8 and 3A4) may alter the pharmacokinetics of Paclitaxel, presenting a theoretical interaction
Clozapine: avoid concomitant use, increased risk of agranulocytosis

References:
UCLH-Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009
UCLH-Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009
Seidman AD et al JCO (2008); 26 (10): 1642-1649
Miller K et al (2007) NEJM; 357: 2666-2676
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