Breast Pathway Group – Paclitaxel weekly in Early Breast Cancer

Indication:  Neoadjuvant or adjuvant alternative therapy to docetaxel, for high risk patients unable to tolerate docetaxel or where there is a contraindication for high dose steroids

Regimen details: Paclitaxel 80 - 90mg/m² IV Day 1

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 12 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

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

Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever.

Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes 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.

©LCA Copyright 2014
Breast Pathway Group – Paclitaxel weekly in Early Breast Cancer

Anti-emetics: Low emetogenicity
Follow local anti-emetic policy

Supportive medication: Not routinely required

Extravasation: Vesicant
Paclitaxel should be administered with appropriate precautions to prevent extravasation. 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

Regular investigations:

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)

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>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.0 &amp;</td>
<td>≥ 100</td>
<td>100% dose</td>
</tr>
</tbody>
</table>
| ≥ 1.0 &               | 75 - 99              | Discuss with Consultant – treatment can be considered on medical advice. Or consider treatment delay for 1 week. Repeat FBC, if platelets recover to ≥ 100 x 10^9/L, resume treatment at 100% dose.

Reason for Update: LCA Protocol Development
Approved by LCA Consultant: Mark Harries

Version: 1.0 Supersedes: all other versions
Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries

Reason for Update: LCA Protocol Development
Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl

Prepared by: Lisa Yuen
Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson

Second check by: Laura Cameron
Date prepared: November 2014
Date revised: November 2016

Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes 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.
©LCA Copyright 2014
Breast Pathway Group – Paclitaxel weekly in Early Breast Cancer

In neoadjuvant/adjuvant treatment, dose reduction and delays can compromise outcome.

- GCSF should be considered if more than one delay and/or before dose reduction. If in doubt, seek Consultant advice.
- If during the preceding cycle, the patient has experienced neutrophils < 0.5 x 10^9/L or has febrile neutropenia diagnosed, GCSF should be considered.
- If despite GCSF treatment, febrile neutropenia occurs or a dose delay is required - seek Consultant advice and consider dose reduction by 25%
- If platelets persistently < 100 x 10^9/L on Day 1 despite dose delay - seek Consultant advice and consider dose reduction by 25%

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>75% 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>

Reason for Update: LCA Protocol Development

Approved by LCA Consultant: Mark Harries

Version: 1.0 Supersedes: all other versions

Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries

Prepared by: Lisa Yuen

Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson

Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes 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.

©LCA Copyright 2014
ARTHRALGIA / 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:**
Outpatient setting
Availability of resuscitation equipment must be ensured as a standard precaution.

**Comments:**
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.

**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 Renal Impairment. January 2009
UCLH- Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009
LCA Breast Cancer Clinical Guidelines October 2013