Paclitaxel, 2 weekly, for Advanced Kaposi Sarcoma

Indication: Second line Palliative therapy, for Advanced Kaposi Sarcoma

Regimen details: Paclitaxel 100mg/m² (*) IV D1

(*) Consultant may consider a 25% dose reduction depending on patient status

Administration: Paclitaxel in 500mls Sodium Chloride 0.9% over 3 hours 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
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: 14 days, for 10 cycles

Extravasation: Paclitaxel: Vesicant

Anti- emetics: Paclitaxel: Low emetogenic
Follow Local Anti-emetic Policy

Regular investigations: FBC D1
LFTs D1
U&Es D1
Clinical toxicity assessment Every 3 cycles

DOSE MODIFICATIONS
Haematological Toxicity

Day1

WBC < 2.0 x 10⁹/L or Neutrophils < 1.0 x 10⁹/L or Platelets < 75 x 10⁹/L

Delay for 1 week.
Repeat FBC - If within normal parameters, resume treatment with 75% Paclitaxel dose

Subsequent cycles

If Neutrophils < 0.5 x 10⁹ / L for ≥ 7 days, OR
Febrile neutropenia is diagnosed OR
Platelets < 50 x 10⁹/ L,
Paclitaxel dose should be reduced to 50% for subsequent cycles and GCSF should be used.

**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>17 - 26</td>
<td>75</td>
</tr>
<tr>
<td>27 – 51</td>
<td>45</td>
</tr>
<tr>
<td>&gt; 51</td>
<td>25</td>
</tr>
</tbody>
</table>

**DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE**

**PERIPHERAL NEUROPATHY – PACLITAXEL**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Neurypathy-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 100mg/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 75mg/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
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
Kobayashi M et al. Internal Medicine (2002); 41:1209-1212
British HIV association guidelines
SELCN Kaposi Sarcoma guidelines 2008
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