Doxorubicin in Advanced, Metastatic or Recurrent Uterine Sarcoma

Indication: Palliative therapy for patients with Advanced, Metastatic or Recurrent Uterine Sarcoma

Regimen details: Doxorubicin  75mg/m² (*)  IV  D1

(*) Consider starting Doxorubicin at 60mg/m² in patients with reduced performance status. Increase dose to 75mg/m² with second cycle only if well tolerated

Administration: Doxorubicin, IV Bolus injection via a fast-running Sodium Chloride 0.9% infusion over 3 – 10 minutes

Frequency: Every 21 days, for a maximum of 6 cycles

Extravasation: Doxorubicin: Vesicant

Anti- emetics: Moderate emetogenic. Follow Local Anti-emetic Policy

Regular investigations: FBC  D1
U&E’s  D1
LFTs  D1
MUGA scan/Echocardiogram Prior to 1st cycle, if necessary (see Comments)
CT scan  After 3 cycles

Comments: Maximum cumulative dose Doxorubicin = 450 - 550mg/m²
A baseline MUGA scan or Echocardiogram should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, diabetes, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy. MUGA scan or Echocardiogram should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum

DOSE MODIFICATIONS

Haematological Toxicity

D1

WBC < 3.0 x 10⁹/L  Delay therapy for 1 week. Repeat FBC – If within normal parameters, proceed with 100% dose

or

Neutrophils < 1.5 x 10⁹/L

or

Platelets < 100 x 10⁹/L

Subsequent cycles

If Neutrophils < 0.5 x 10⁹ / L for ≥ 7 days, OR
Febrile neutropenia is diagnosed OR
Platelets < 50 x 10⁹/L,
Doxorubicin dose should be reduced to 60mg/m² from previous dose. If the patient continues to experience these side effects at the lower dose, discontinue therapy
Renal Impairment: Doxorubicin: Dose reduction in severe renal impairment (GFR < 10 ml/min) should be discussed with the Consultant.

Hepatic Impairment: Doxorubicin dose should be adjusted as follows:

<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>Doxorubicin Dose</th>
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<tbody>
<tr>
<td>&lt; 20</td>
<td>Give 100%</td>
</tr>
<tr>
<td>20 – 50</td>
<td>Give 50%</td>
</tr>
<tr>
<td>51 – 85</td>
<td>Give 25%</td>
</tr>
<tr>
<td>&gt; 85</td>
<td>Omit</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AST/ ALT (units)</th>
<th>Doxorubicin Dose</th>
</tr>
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<tbody>
<tr>
<td>2 – 3 x normal</td>
<td>Give 75%</td>
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</tbody>
</table>

Toxicities: Myelosuppression; fatigue; nausea; vomiting; constipation; diarrhoea; mucositis; cardiotoxicity; alopecia.

Drug interactions: Doxorubicin
- Ciclosporin (high dose) increase Doxorubicin serum levels and myelotoxicity
- Clozapine: increased risk of agranulocytosis, avoid concomitant use
- Concomitant use of other cardioactive compounds e.g. calcium channel blockers require monitoring of cardiac function throughout treatment
- Digoxin tablets: reduced absorption (resolved by giving the digoxin in liquid)
- Quinolones: antimicrobial effect of quinolones decreased
- Phenytoin: reduced absorption of the antiepileptic
- Warfarin: the anticoagulant effect is increased

References: www.medicines.org.uk
Santoro A et al. JCO (1995); 13: 1537 - 1545
COIN Guidelines. October 2000
UCLH- Dosage Adjustment for Cytotoxics in Renal Impairment. November 2003
UCLH- Dosage Adjustment for Cytotoxics in Hepatic Impairment. November 2003
GSTT guidelines for treating nausea and vomiting in adult patients. September 2007
CTCAE v3.0. August 2006