Systemic Anti Cancer Treatment Protocol

Cisplatin Doxorubicin
Sarcoma

PROCEDURE REF: MPHACISDOX
(Version No. _1.0)

Approved for use in:

Osteosarcoma – Palliative / advanced disease
Not suitable for PAM schedule for operable osteosarcoma (see separate PAM protocol for AP part of PAM)
De-differentiated chondrosarcoma
Chordoma
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Dosage:

Drug	Dosage	Route	Frequency
Cisplatin	100mg/m^2	IV	Every 21 days
Doxorubicin	25mg/m^2 days 1,2,3	IV	Every 21 days

Consider doxorubicin 20mg/m^2/days 1, 2 and 3 for patients > 60yrs

Supportive treatments:
Filgrastim for surgical patients

Anti-emetic risk - high
Dexamethasone tablets, 4mg twice daily for 3 days
Domperidone 10mg oral tablets, up to 3 times a day or as required

Extravasation risk:

Cisplatin – Irritant
Doxorubicin – vesicant – follow trust/network policy, specific treatment may apply

Administration:

Day	Drug	Dosage	Route	Diluent and Rate
1	**Aprepitant** 30 mins before doxorubicin	125mg	PO	
1	**Dexamethasone** 30 mins before doxorubicin	12mg	PO	
1	**Ondansetron** 30 mins before doxorubicin	16mg	PO	
1	**Doxorubicin**	25mg/m^2	IV	Continuous infusion over 24 hours in 100mL sodium chloride 0.9%
1	Sodium Chloride 0.9% 1000mL with 20mmol Potassium Chloride and 10mmol Magnesium Sulphate	1000mL	IV	Over 2 hours
1	**Measure urine output volume and record** **If urine output averages 100mL/hour over previous 3 hours then proceed with cisplatin infusion** **If urine output is less than 100mL/hour the patient should be assessed and further 500mL sodium chloride 0.9% given IV over 30 minutes** **If urine output still not adequate contact the medical team**			
1	**Cisplatin**	100 mg/m^2	IV	In 1000mL 0.9% Sodium Chloride over 4 hours
	Sodium Chloride 0.9% 1000mL with 20mmol Potassium Chloride and 10mmol Magnesium Sulphate	1000mL	IV	Over 4 hours
2	**Aprepitant** 30 mins before doxorubicin	80mg	PO	Give 24 hours after day 1 dose
2	**Dexamethasone** 30 mins before doxorubicin	12mg	PO	
2	**Ondansetron** 30 mins before doxorubicin	16mg	PO	
2	**Doxorubicin**	25mg/m^2	IV	Continuous infusion over 24 hours in 100mL sodium chloride 0.9%
3	**Aprepitant** 30 mins before doxorubicin	80mg	PO	Give 24 hours after day 2 dose
3	**Dexamethasone** 30 mins before doxorubicin	12mg	PO	
3	**Ondansetron** 30 mins before doxorubicin	16mg	PO	
3	**Doxorubicin**	25mg/m^2	IV	Continuous infusion over 24 hours in 100mL sodium chloride 0.9%

Alternatively, doxorubicin can be administered as IV bolus, 25mg/m^2 on days 1, 2 and 3 at 24 hour intervals.

Patients will require double lumen PICC line (or equivalent)

Hydration for cisplatin to commence at same time as doxorubicin infusion

At the end of IV fluids:

- Weigh the patient and review fluid balance chart
- If there is a positive balance of 1.5L or 1.5kg in weight gained then consider furosemide 20mg orally and review output after 30 minutes. Any concerns then discuss with medical team prior to discharging the patient.

PAM alternative – give every 21 days for 3 cycles followed by surgery then give a further 3 cycles every 21 days

Advanced disease – give every 21 days for 6 cycles

Notes:

Cisplatin

The patient should be asked to drink 2 litres of fluid over 24 hours after the infusion and should contact the unit immediately if unable to do so for any reason.

Doxorubicin

Maximum cumulative dose of doxorubicin: 450 to 550mg/m^2
Perform baseline MUGA if patient is considered at risk of significantly impaired cardiac contractility.
Use alternative regimen if cardiac ejection fraction < 50%
Repeat MUGA during treatment if there is any suspicion of cardiac impairment

Main Toxicities:

Cisplatin – myelosuppression, neuropathy, ototoxicity, nephrotoxicity, alopecia (mild)

Doxorubicin - Myelosuppression, alopecia, mucositis, cardiomyopathy (see notes and treatment plan), ovarian failure / infertility

Investigations and treatment plan

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Comments
Medical Assessment	X	X	X	X	X	X	X	
Nursing Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	X	X	Every cycle
Mg2+ and Ca2+	X	X	X	X	X	X	X	Every cycle
CrCl (Cockroft and Gault)	X	X	X	X	X	X	X	Every cycle
CT scan	X		X					As clinically indicated
MUGA/ECHO	X							If clinically indicated
Informed Consent	X							
Blood pressure measurement	X	X	X	X	X	X	X	As clinically indicated
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if all apply:

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Delay 1 week on day 1 if any apply:-

ANC ≤ 0.9 x 10^9/L	Platelets ≤ 99 x 10^9/L

Surgical patients: it is essential patients stay on schedule before and after surgery. Discuss any delays or dose alterations with consultant first.

Non-haematological toxicity

<table>
<tr><td>Renal</td><td>Cisplatin is eliminated primarily (>90%) in the urine and is itself nephrotoxic. If there is any significant renal toxicity discuss with consultant before proceeding.
Calculate CrCl before the start of treatment using Serum Creatinine and Cockroft and Gault. If the result is borderline consider EDTA clearance. Recalculate CrCl using Cockroft and Gault every cycle and consider EDTA if serum creatinine varies by more than 30% from baseline.
<table>
<tr><th>GFR (mL/min)</th><th>Cisplatin dose</th></tr>
<tr><td>Above 50</td><td>100% dose</td></tr>
<tr><td>40 to 50</td><td>75% dose</td></tr>
<tr><td>Below 40</td><td>Contra indicated – Do not give</td></tr>
</table>
No modifications needed for doxorubicin</td></tr>
<tr><td>Hepatic</td><td>
<table>
<tr><th>Bilirubin (µmol/L)</th><th>Doxorubicin dose</th></tr>
<tr><td>20 to 50</td><td>50%</td></tr>
<tr><td>51 to 85</td><td>25%</td></tr>
<tr><td>Above 85</td><td>omit</td></tr>
<tr><td>AST</td><td></td></tr>
<tr><td>2 to 3 x ULN</td><td>75%</td></tr>
<tr><td>Above 3 x ULN</td><td>50%</td></tr>
</table>
No modifications needed with cisplatin</td></tr>
</table>

Cisplatin

Neuro or Ototoxicity	Note baseline audiometry If any signs of either refer to consultant before proceeding

Doxorubicin

Mucositis	Grade 3 to 4 reduce doxorubicin dose to 20mg/m^2/day
Cardiomyopathy	Perform baseline MUGA in any patient with suspected cardiac impairment. If cardiac ejection fraction < 50% discuss with consultant and consider an alternative regimen. Consider a lower maximum cumulative doxorubicin dose of 400mg/m^2 for any patient with cardiac dysfunction or that has been exposed to mediastinal radiation Note that cardiomyopathy may be delayed – if 20% reduction if LVEF after 300mg/m^2 then stop doxorubicin

References:

Souhami et al. Lancet 1997 Sep 27; 350:911-7