Regimen : Cisplatin and Radiotherapy for Head and Neck Cancers

### Indication
Chemo-radiation for head and neck cancers

### Regimen details
<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cisplatin</td>
<td>40 mg/m²</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Max dose 70mg)</td>
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</tr>
</tbody>
</table>

### Administration

**Pre-hydration:**
1000mls Sodium Chloride 0.9% with 20 mmol KCL and 2g MgSO₄ over 2 hours, followed by Mannitol 20% 100ml over 10 min OR Mannitol 10% 200ml over 15 min

*Cisplatin* in 500ml Sodium Chloride 0.9% over 60 minutes

**Post-hydration:**
Sodium Chloride 0.9% 1000mls with 20 mmol KCL and 2g MgSO₄ over 2 hours

Note: Patients with low Magnesium levels (<0.7 mmol/l) should have an additional 2g magnesium sulphate added to the pre-hydration bag

### Frequency
Weekly for a maximum of 6 weeks during radical radiotherapy

### Extravasation
Exfoliant (Group 4)

### Premedication
Pre-hydration as above

### Emetogenicity
This regimen has moderate-high emetogenic potential – refer to local protocol

### Additional recommended supportive medication
If magnesium levels are consistently low, consider supplementation with oral magnesium glycerophosphate [Note: unlicensed product] 24 mmol Mg²⁺ per day in divided doses.

### Pre-treatment evaluation
- **FBC**: Baseline – results valid for 14 days
- **U+E**: Baseline – results valid for 14 days
- **LFT**: Baseline – results valid for 14 days

### Regular investigation
- **FBC**: Results valid for 72 hrs
- **U+E**: Results valid for 72 hrs
- **LFT**: Results valid for 72 hrs

### Standard limits for administration to go ahead – if blood results not within range, authorisation to administer must be given by prescriber/consultant
- **Neutrophil count**: 1.5 x 10⁹/L
- **Platelet count**: 100 x 10⁹/L
- **Haemoglobin**: 10 x g/dL (However if Hb<12 g/dL a 2 unit blood transfusion should be arranged)
- **Creatinine clearance**: ≥ 45 ml/hour
- **Bilirubin**: <1.5 x ULN
### Dose modifications

#### Haematological toxicity
Defer chemotherapy for 1 week if neutrophils $< 1.5 \times 10^9/L$ or platelets $< 100 \times 10^9/L$

#### Renal impairment

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Cisplatin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>100%</td>
</tr>
<tr>
<td>50-59</td>
<td>75%</td>
</tr>
<tr>
<td>&lt;50</td>
<td>Consider Cetuximab</td>
</tr>
</tbody>
</table>

Or substitute with (a) Cetuximab or (b) Carboplatin AUC 2

#### Hepatic impairment
No dose reduction necessary.

### NCI Common toxicity criteria

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Definition</th>
<th>Dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotoxicity</td>
<td>Grade 2</td>
<td>Reduce dose to 30mg/m²</td>
</tr>
<tr>
<td></td>
<td>Grade 3-4</td>
<td>Discontinue Cisplatin</td>
</tr>
<tr>
<td>Ototoxicity</td>
<td>Grade 2</td>
<td>Reduce dose to 30mg/m²</td>
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<td></td>
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### Toxicity Definition Dose adjustment

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<td>Grade 2</td>
<td>Myelosuppression and risk of</td>
<td>Reduce dose to 30mg/m²</td>
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<tr>
<td></td>
<td>sepsis</td>
<td>Discontinue Cisplatin</td>
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</tbody>
</table>

**Neurotoxicity**
- Grade 2: Myelosuppression and risk of sepsis
- Grade 3-4: Reduce dose to 30mg/m²
- Grade 4: Discontinue Cisplatin

**Ototoxicity**
- Grade 2: Reduce dose to 30mg/m²
- Grade 3-4: Discontinue Cisplatin

### Adverse effects

<table>
<thead>
<tr>
<th>Rare or serious side effects</th>
<th>Frequently occurring side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelosuppression and risk of sepsis</td>
<td>Nausea/vomiting</td>
</tr>
<tr>
<td>Nephrotoxicity</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Ototoxicity</td>
<td>Constipation</td>
</tr>
<tr>
<td></td>
<td>Mucositis</td>
</tr>
<tr>
<td></td>
<td>Peripheral neuropathy</td>
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<tr>
<td></td>
<td>Alopecia</td>
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<tr>
<td></td>
<td>Fatigue</td>
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<tr>
<td></td>
<td>Electrolyte disturbances</td>
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</tbody>
</table>

### Significant drug interactions

- Allopurinol, colchicine, probenecid, sulfinpyrazone: increase in serum uric acid concentration
- Cephalosporins, aminoglycosides, amphotericin B: increase nephrotoxic and ototoxic effects of cisplatin when administered simultaneously or 1-2 weeks after treatment with cisplatin.
- Ciclosporin: excessive immunosuppression, with risk of lymphoproliferation
- Cyclizine, phenothiazines: may mask ototoxicity symptoms
- Furosemide, hydralazine, diazoxide and propranolol: intensify nephrotoxicity
- Oral anticoagulants: require an increased frequency of the INR monitoring
- Penicillamine: may diminish the effectiveness of cisplatin
- Phenytoin: reduced serum levels of phenytoin (due to reduced absorption and/or increased metabolism) can reduce epilepsy control-monitor phenytoin levels in these patients.

### Comments
None

### Cumulative Doses
Not applicable

### References

- Bachaud, J-M, Cohen-Jonathan E, Alzieu C, David J-M, Serrano E, Daly-Schweitzer N. Combined postoperative radiotherapy and Weekly Cisplatin infusion for locally advanced...


