B5 GI Cancer Protocols

B5.1 Cisplatin- and 5-Fluorouracil (5-FU)

B5.1.1 Indication
- Head and neck, oesophageal and anal cancer:-
- Palliative therapy for stage IV or relapsed disease
- 2 cycles as induction therapy prior to surgery or definitive irradiation
- Concomitant chemo-irradiation for oesophageal and anal cancer

B5.1.2 Pre treatment evaluation
- Multi-disciplinary review and histological confirmation
- Investigations should include CT scan of chest, and upper abdomen
- Record WHO performance status, current height, weight and surface area
- FBC, U&E, serum creatinine, LFTs
- Ensure that calculated creatinine clearance >55mls/min (refer to renal dose modification table)
- Consider formal measurement of creatinine clearance in patients with low surface area or poor renal function using either 24-hour urine collection or EDTA measurements.
- Document evaluable disease
- Give adequate verbal and written information for patients and relatives concerning patient’s disease, treatment strategy and side effects/mortality risk.
- Obtain written consent from patient or guardian.
- If appropriate, discuss potential risk of infertility/early menopause with patient and relatives.

B5.1.3 Drug Regimen

<table>
<thead>
<tr>
<th>Days</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cisplatin</td>
<td>80mg/m²</td>
<td>IV</td>
<td>IV infusion in 500ml Sodium Chloride 0.9% over 60 minutes with pre and post hydration†</td>
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<tr>
<td>1 to 4</td>
<td>5-Fluorouracil (5-FU)</td>
<td>1000mg/m²/day*</td>
<td>IV</td>
<td>IV infusion in 1000ml Sodium Chloride 0.9% over 22h daily for 4 days or by continuous infusion via ambulatory pump</td>
</tr>
</tbody>
</table>

† Refer to ASWCS Individual Drug Guidelines for specific recommendations when administering Cisplatin (Section A3.2)
B5.1.4 Additional Modifications

* If serious line complications and/or for palliative therapies substitute 5-FU for Capecitabine 625 mg/m² twice daily continuously (total dose: 1250mg/m²/day)

B5.1.5 Dose Modifications

B5.1.5.1 Haematological

Defer therapy for 1 week if neutrophils <1.0 x 10⁹/l or platelets < 100 x 10⁹/l

B5.1.5.2 Renal Function

<table>
<thead>
<tr>
<th>GFR ml/min</th>
<th>Cisplatin Dose</th>
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<tbody>
<tr>
<td>&gt; 55</td>
<td>100%</td>
</tr>
<tr>
<td>40 – 55</td>
<td>Either / or</td>
</tr>
<tr>
<td></td>
<td>Substitute with Carboplatin</td>
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<tr>
<td></td>
<td>AUC x5</td>
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<tr>
<td></td>
<td>Cisplatin dose</td>
</tr>
<tr>
<td></td>
<td>mg=mls/min clearance</td>
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<tr>
<td>&lt; 40</td>
<td>Substitute with Carboplatin (Carboplatin Contra-indicated if GFR &lt;20ml/min)</td>
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Although there is experience of using the same dose of Cisplatin as the Creatinine Clearance (CrCl) (i.e. 1mg/ml/min GFR, there is no evidence to support this practice)

Dose reduce 5FU in severe renal impairment only

B5.1.5.3 Hepatic Function

- Omit treatment if bilirubin > 85 umol/L unless secondary to biliary obstruction
- In moderate hepatic impairment, consider giving 33% dose reduction for 5-FU during initial doses
- In severe hepatic impairment, consider giving 50% dose reduction for 5-FU during initial doses
- Increase 5-FU dose if no toxicity

B5.1.5.4 Other Non-Haematological Dose Modifications

- Dose reductions for stomatitis and diarrhoea are based on dose given in preceding cycle and continue for remaining cycles. If multiple toxicities are seen, the dose administered is based on the most severe toxicity experienced.
- If patient has ≥ Grade II stomatitis diarrhoea, 5-FU must NOT be given, defer 1 week until toxicity has resolved to ≤ Grade I toxicity
- If Grade 1 manage symptomatically with Loperamide and/or Codeine Phosphate
- If Grade 2 diarrhoea or stomatitis reduce 5-FU dose by 20% for all subsequent treatments
- If Grade 3 add in Ciprofloxacin 250 mg bd, and consider 50% dose reduction
- If Grade 4, discontinue treatment

**B5.1.5 Antiemetics/supportive therapy**
- This regimen has severe emetic potential - refer to local protocol
- Give warfarin 1mg od to lessen thrombotic complications to all patients receiving infusional 5-FU. Fully anticoagulate if shoulder pain develops
- Give Benzydamine (Difflam®) mouthwash and Loperamide (Imodium® equivalent) to all patients for prn use
- Sucralfate suspension mouthwash (5-10ml qds) is useful for sore mouths
- Pyridoxine 50 mg tds reduces the severity of plantar-palmar erythema

**B5.1.6 Cycle frequency**
- 21 days usually no more than 4 courses

**B5.1.7 Adverse effects**
- Nausea/vomiting
- Mucositis
- Stomatitis
- Constipation and/or diarrhoea
- Mild to Moderate alopecia
- Line thrombus
- Renal toxicity
- Electrolyte Imbalance (especially hypomagnesaemia and hypocalcaemia)
- Hypersensitivity Reactions
- Palmar-plantar erythema (Hand-Foot Syndrome)
- Peripheral neuropathy
- Myelosuppression and risk of sepsis and thrombocytopenia
- Skin changes, sore eyes and runny nose
- Rare vascular toxicity including angina & cardiac spasm

**B5.1.8 Investigations Prior to Subsequent Cycles**
- Before each course check FBC, U&Es (including magnesium & calcium), serum creatinine, LFTs
- Clinical toxicity assessment (including stomatitis)

**B5.1.9 References**

BOPA Treatment Guideline “Dosage Adjustment for Cytotoxics in Renal Impairment” [http://www.bopa-web.org/Members/Guidelines]

BOPA Treatment Guideline “Dosage Adjustment for Cytotoxics in Hepatic Impairment” [http://www.bopa-web.org/Members/Guidelines]

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<th>Written by:</th>
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<td>Authorised By:</td>
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<tr>
<td>Chair ASWCS Pharmacists Group</td>
<td>Chair ASWCS Nursing Group</td>
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