MITOMYCIN C, 5-FLUOROURACIL + RADIOTHERAPY

Squamous cell carcinoma of the anus
This regimen also occasionally used for scc of penis

Drug/Dosage:
5-Fluorouracil 1000mg/m²/24hr  IV  D1 - D4 and D29 – D32
Mitomycin C  12mg/m²  IV  D1 of Week 1 only

Patients aged > 70 years, or those with significant co-morbidity:
5-Fluorouracil 750mg/m²/24hr  D1 – D4 and D29 – D32
Mitomycin C  10mg/m²  D1 of Week 1 only

Radiotherapy:
Radiotherapy is delivered over 5 – 6 weeks on weekdays only, with concurrent chemotherapy during the first and fifth week. It is stressed that Week 5 of RT must be accompanied by the second course of 5FU.

Administration:
Mitomycin C via fast running infusion of 0.9% sodium chloride
5FU is to be started at least 2 hours prior to first fraction of RT
5FU continuous IV infusion over 4 days, given via CVC and ambulatory infusion device

Frequency:
Week 1 and Week 5: chemo-radiotherapy
Weeks 2, 3 and 4: radiotherapy only
Clinical review weekly

Main toxicities:
myelosuppression; mucositis; diarrhoea; palmar/plantar erythema
radiation fibrosis / necrosis of perineum; haemolytic uraemic syndrome;
coronary artery spasm (see Comments); ovarian failure/infertility;
impotence (males); urinary frequency/cystitis

Anti-emetics:
moderately emetogenic

Extravasation:
mitomycin C is a vesicant

Regular Investigations:
FBC  weekly (N.B. see Dose Modifications for Hb monitoring)
LFTs  Day 1 of Week 1 & Day 1 of Week 5
U&Es  Day 1 of Week 1 & Day 1 of Week 5

Comments:
Maximum cumulative dose of mitomycin C = 28mg/m² or 56mg total dose.

Haemolytic uraemic syndrome is a complication of mitomycin C. Therefore, monitor renal function carefully and request Red Cell Fragments on peripheral blood films if in doubt.

Coronary artery spasm is a recognised complication of 5FU although the evidence base regarding aetiology, management and prognosis is not particularly strong. The incidence is estimated to be between 2% and 18%. Coronary artery spasm is more common in patients receiving continuous infusions of 5FU, and is usually reversible on discontinuing the infusion. Should a patient receiving 5FU present with chest
pains, stop the 5FU. Standard investigation and treatment of angina may be required. If re-challenge is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, the 5FU should be withdrawn permanently.\(^1\) Refer to Consultant to discuss.

### Dose Modifications

**Haematological Toxicity:**

- WBC $< 3.0 \times 10^9/l$
- Neutrophils $< 1.5 \times 10^9/l$
- Platelets $< 100 \times 10^9/l$

**NB. Chemotherapy must not be delayed without Consultant approval**

Clinical decision for individual situation.

If appropriate, proceed, followed by G-CSF support starting on day after 5FU infusion completed. If in doubt, discuss with Consultant.

Haemoglobin (Hb) needs to be maintained above 12g/dl throughout this treatment. If the Hb falls below this level, a blood transfusion needs to be arranged (treatment may continue).

**Renal Impairment:**

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Mitomycin C Dose</th>
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<tbody>
<tr>
<td>$&gt; 10$</td>
<td>Give 100%</td>
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<tr>
<td>$&lt; 10$</td>
<td>Give 75%</td>
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**Hepatic Impairment:**

- Moderate hepatic impairment: Reduce initial 5FU dose by $\frac{1}{3}$
- Severe hepatic impairment: Reduce initial 5FU dose by $\frac{1}{2}$

Dose can be increased if no toxicity seen. If in doubt, check with the relevant Consultant.

**Other Toxicities:**

If Grade 3/4 mucositis, PPE or diarrhoea occurs, the dose of 5 FU should be reduced to 750mg/m\(^2\)/24hrs for Week 5.

*For any Grade 4 toxicity, discuss with Consultant before proceeding.*

**References:**

- James, RD et al; Lancet Oncology 2013; published online April 9 (ACT II trial)
- \(^1\)COIN Guidelines Oct 2000