MITOMYCIN C / 5-FLUOROURACIL + RADIOTHERAPY

Chemo-radiotherapy for muscle invasive bladder cancer

Drug/Dosage:  5-Fluorouracil  500mg/m²/24hr IV  Day 1 – 5 and Day 22 – 26
              (Days 1 – 5 of Week 1 and Week 4 of radiotherapy)

              Mitomycin C  12mg/m²  IV  D1 of Week 1 only

Radiotherapy:  64Gy/32# given Monday–Friday for 6.5 consecutive weeks.

It is stressed that Week 4 of RT must be accompanied by the second week 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 5 days, given via CVC and ambulatory infusion device

Frequency:  Week 1 and Week 4: Chemo-radiotherapy
            Weeks 2, 3, 5 and 6: Radiotherapy only
            Clinical review weekly

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

Anti-emetics:  Day 1 of Week 1: moderately emetogenic; Days 2-5 of Week 1: mildly emetogenic
               Days 1-5 of Week 4: mildly emetogenic

Extravasation:  mitomycin C is a vesicant

Regular Investigations:
                FBC  weekly (Hb should be kept > 12g/dl)
                LFTs  Day 1 of Week 1 & Day 1 of Week 4
                U&Es  Day 1 of Week 1 & Day 1 of Week 4

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is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, the 5FU should be withdrawn permanently. Refer to Consultant to discuss.
Dose Modifications

Haematological Toxicity:

- WBC < 3.0 x 10^9/l
- Neutrophils < 1.5 x 10^9/l
- Platelets < 100 x 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) should 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:

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<tr>
<th>CrCl (ml/min)</th>
<th>Mitomycin C Dose</th>
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<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 1/3
- Severe hepatic impairment: Reduce initial 5FU dose by 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 5FU dose should be reduced to 375mg/m^2/24hrs for Week 4.

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

References:

2. James, ND et al; JCO 2010; 28: 15s (suppl); abstract 4517
3. COIN Guidelines Oct 2000