MITOMYCIN C / 5-FLUOROURACIL + RADIOTHERAPY

Chemo-radiotherapy for muscle invasive bladder cancer

Drug/Dosage:	5-Fluorouracil	500mg/m^2/24hr	IV	Day 1 – 5 and Day 22 – 26 (Days 1 – 5 of Week 1 and Week 4 of radiotherapy)
	Mitomycin C	12mg/m^2	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/m^2 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is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, the 5FU should be withdrawn permanently.[1] Refer to Consultant to discuss.

Reason for Update: peripheral 5FU infusion removed	Approved by Consultant: Dr J Money-Kyrle
Version: 2	Approved by Lead Chemotherapy Nurse: V Mumford
Supersedes: Version 1	Date: 30.12.13
Prepared by: S Taylor	Checked by: C Tucker

Dose Modifications

Haematological Toxicity:	WBC < 3.0 x 10^9/l or Neutrophils < 1.5 x 10^9/l or 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:

CrCl (ml/min)	Mitomycin C Dose
> 10	Give 100%
< 10	Give 75%

Hepatic Impairment:

Moderate hepatic impairment	Reduce initial 5FU dose by 1/3
Severe hepatic impairment	Reduce initial 5FU dose by ½

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: Hussain, SA et al; Br J Cancer 2004; 90 (11): 2106 – 2111
James, ND et al; JCO 2010; 28: 15s (suppl); abstract 4517
[1]COIN Guidelines Oct 2000