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/m^2/24hr	IV	D1 - D4 and D29 – D32
	Mitomycin C 12mg/m^2	IV	D1 **of Week 1 only**
	Patients aged > 70 years, or those with significant co-morbidity:		
	5-Fluorouracil 750mg/m^2/24hr		D1 – D4 and D29 – D32
	Mitomycin C 10mg/m^2		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/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is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, the 5FU should be withdrawn permanently.[1] Refer to Consultant to discuss.

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) 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:

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 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