MITOMYCIN FLUOROURACIL with concurrent radiotherapy

INDICATION (ICD10) C21
1. Anal cancer (unlicenced). PS 0, 1, 2

REGIMEN

Day 1	**MITOMYCIN**	12mg/m^2* (maximum 20mg)	IV bolus	
Days 1 and 29	**FLUOROURACIL**	4000mg/m^2*	IV infusion	continuous over 96 hours

*Fluorouracil dose may be decreased to 3000mg/m^2 and/or mitomycin dose may be decreased to 10mg/m^2 if >70 years based on clinical decision

CYCLE FREQUENCY AND NUMBER OF CYCLES
One cycle for duration of RT (5.5 weeks) only

ANTI-EMETICS
Low emetogenic risk

CONCURRENT MEDICATION REQUIRED

Fluorouracil	Mouth and bowel support eg loperamide, benzydamine mouthwash Prophylactic antibiotics eg ciprofloxacin 250mg bd for 8 weeks during chemoradiotherapy and until skin reactions have settled in view of MHRA alert consultant confirmation required

EXTRAVASATION AND TYPE OF LINE / FILTERS
Fluorouracil - inflammitant
Mitomycin - vesicant

Central line (single lumen)

INVESTIGATIONS
Blood results required before SACT administration

FBC, U&E and LFTs Neutrophils ≥1.5x10^9/L Platelets ≥100x10^9/L	baseline and every cycle
EDTA GFR or calculated CrCl at consultant's discretion.	baseline and every cycle
Serum creatinine	baseline and every cycle
DPYD (dihydropyrimidine dehydrogenase) test	baseline
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Fluorouracil	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds. Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function (consider ECG at baseline). Special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil. Stomatitis
Mitomycin	Allergic skin rash, contact dermatitis, palmar-plantar erythema, pruritus. Cystitis (possibly haemorrhagic), dysuria, nocturia, pollakiuria, haematuria, local irritation of the bladder wall.

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Fluorouracil	Cimetidine slightly increases exposure to fluorouracil Metronidazole increased toxicity Phenytoin concentration increased Warfarin

DOSE MODIFICATIONS
Mitomycin maximum lifetime dose =28-36mg/m^2
DPYD variant identified follow national or local DPD dose modification guidelines.

Fluorouracil
The fluorouracil course should be delayed for a week or until completely recovered in the event of either low blood counts (neutrophils <1.5x10^9 or platelets <100x10^9) or any persistent mucositis or diarrhoea.

Non-haematological toxicity (CTC grade): diarrhoea, stomatitis	0-1	2	3	4
Haematological toxicity (x10^9/L): Platelets ≥50 and neutrophils ≥1.0	100%	80%	50%	No further treatment
Haematological toxicity (x10^9/L): Platelets 25-49 or neutrophils 0.5-0.9	80%	70%	50%	No further treatment
Haematological toxicity (x10^9/L): Platelets <25 or neutrophils <0.5	50%	50%	50%	No further treatment

Hepatic impairment
Fluorouracil

Significantly impaired hepatic function eg bilirubin >50micromol/L may be a sign of disease progression and require cessation of, or change in, treatment. Always discuss deteriorating liver function with consultant.	
If hepatic function is impaired, the recommended dose can be reduced to give 50% to 70% dose, but no need for dose adjustment is expected in mild and moderate (without renal impairment).	
Bilirubin >85micromol/L	not recommended

Mitomycin

Mild and moderate	no need for dose adjustment expected.
Severe	consider 50% of original dose.

Renal impairment
Fluourouracil

If renal function is impaired, the recommended dose can be reduced to give 50% to 70% dose, but no need for dose adjustment is expected.

Mitomycin

CrCl ≥30ml/min	give 100% dose
CrCl <30ml/min	not recommended

REFERENCES

Assessment

	Cycle 1				Subsequent cycles			Comments
	Pre	Day 1	Day 22	Day 29	Day 1	Day 22	Day 29	
Clinical assessment	X				X			Every 3 months and as clinically indicated
SACT assessment (PS and toxicities)	X	X	X		X	X		Every cycle
FBC	X		X	X	X	X	X	Every cycle
U&E & LFT	X		X	X	X	X	X	Every cycle
Dihydropyrimidine dehydrogenase (DPYD) deficiency test	X							This test is required for every patient newly started on capecitabine or fluorouracil. The result MUST be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary.
Informed consent	X							
Weight recorded	X	X			X	X		