MITOMYCIN CAPECITABINE

INDICATION (ICD10) C18, C20

1. Advanced colorectal cancer (unlicensed). PS 0, 1, 2

REGIMEN

Day 1	**MITOMYCIN**	7mg/m^2	IV bolus	
Days 1 to 14 and 22 to 35	**CAPECITABINE**	1250mg/m^2* (2500mg/m^2/day)	oral	twice daily

*1000mg/m^2 may be used

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 42 days for 4 cycles (review after 2 cycles)

ANTI-EMETICS

Low risk days 1 to 14 and 22 to 35

CONCURRENT MEDICATION REQUIRED

Capecitabine	Mouth and bowel support eg loperamide, benzydamine mouthwash

ADMINISTRATION

Capecitabine	should be taken 12 hours apart. Swallowed with water within 30 minutes after a meal, or dissolve in 200ml luke warm water, stir thoroughly (squash may be added if unpalatable).

EXTRAVASATION AND TYPE OF LINE / FILTERS

Mitomycin - vesicant

Peripheral line

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

Capecitabine	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function. To minimise risk of anthracycline induced cardiac failure signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. All patients should be told to report any cardiac symptoms immediately and should be told to stop the medication immediately if any suspicion of cardiac problems. 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)

Capecitabine	Brivudine and analogues should be avoided Warfarin and caution with all oral anticoagulants Phenytoin Allopurinol

DOSE MODIFICATIONS

Mitomycin maximum lifetime dose =28-36mg/m^2

DPYD variant identified follow national or local DPD dose modification guidelines.

Non-haematological

Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction).

Once the dose has been reduced it should not be increased at a later time.

When capecitabine is stopped for toxicity, the doses are omitted and not delayed.

Toxicity grades	Dose changes within a treatment cycle	Dose adjustment for next cycle/dose (% of starting dose)
Grade 2 - 1st appearance	Interrupt until resolved to grade 0-1	100%
Grade 2 - 2nd appearance	Interrupt until resolved to grade 0-1	75%
Grade 2 - 3rd appearance	Interrupt until resolved to grade 0-1	50%
Grade 2 - 4th appearance	Discontinue treatment permanently	Not applicable
Grade 3 - 1st appearance	Interrupt until resolved to grade 0-1	75%
Grade 3 - 2nd appearance	Interrupt until resolved to grade 0-1	50%
Grade 3 - 3rd appearance	Discontinue treatment permanently	Not applicable
Grade 4 - 1st appearance	Discontinue permanently OR if physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1	50%
Grade 4 - 2nd appearance	Discontinue treatment permanently	Not applicable

Hepatic impairment

Capecitabine

Bilirubin of >3xULN or ALT/AST >2.5xULN	Interrupt capecitabine Treatment may be resumed when bilirubin decreases to <3xULN or hepatic aminotransferases decrease to <2.5xULN.

Mitomycin

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

Renal impairment

Capecitabine

CrCl >50ml/min	give 100% dose
CrCl (ml/min) 30-50ml/min	give 75% dose
CrCl (ml/min) <30ml/min	contraindicated

Mitomycin

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

REFERENCES

1. Br J Cancer. 2006 Mar 27;94(6):935-6

Assessments

	Pre	Cycle 1		Subsequent cycles		Comments
		Day 1	Day 22	Day 1	Day 22	
Informed consent	x					
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	Every cycle
U&E & LFTs	x		x	x	x	Every cycle
CrCL	x		x	x	x	
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.
CT scan	x				Check CT ordered on last cycle	
Weight recorded	x	x		x		
Urine dipstick for protein / RBC	x			x		