MITOMYCIN Modified de Gramont

INDICATION (ICD10) C18, C20

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

REGIMEN

Mitomycin to be given first

Day 1	**MITOMYCIN**	6mg/m^2	IV bolus	
	CALCIUM FOLINATE	350mg	IV infusion	250ml glucose 5% over 30 minutes
	FLUOROURACIL	400mg/m^2	IV bolus	
	FLUOROURACIL	2400mg/m^2	IV infusion	continuous over 46 hours
Day 15	**CALCIUM FOLINATE**	350mg	IV infusion	250ml glucose 5% over 30 minutes
	FLUOROURACIL	400mg/m^2	IV bolus	
	FLUOROURACIL	2800mg/m^2	IV infusion	continuous over 46 hours

diluent and diluent volume for dose prescribed as per national standardised product specification

NB Calcium folinate (calcium leucovorin) is not the same as calcium levofolinate.
Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of calcium folinate.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days for 3 to 6 cycles (review after 3 cycles)

ANTI-EMETICS

Low emetogenic risk days 1 and 15

CONCURRENT MEDICATION REQUIRED

Fluorouracil	Mouth and bowel support eg loperamide, benzydamine mouthwash

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 days 1 and 15 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.

Haematological

Neutrophils <1.5x10^9/L and/or platelet count <100x10^9/L	delay one week, recheck blood count

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

1. FOCUS (CR08) clinical protocol 2001
2. Calcium levofolinate SPC 06/2002 www.medicines.org.uk
3. Bunn R & Ashley C, The Renal Drug Handbook Radcliffe Medical Press, Oxford;1999:61

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Alternate cycles or team discretion
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E, calcium, & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
Dihydropyrimidine dehydrogenase (DPYD) deficiency test	X					This test is normally only required if a patient has not had capecitabine or fluorouracil in the past. However a consultant may still request this test if capecitabine or fluorouracil was not tolerated previously. The result MUST be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary.
CT scan	X					Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle