CAPECITABINE AND MITOMYCIN C

Metastatic colorectal cancer resistant to 5FU and Irinotecan

Drugs/Dosage:	Capecitabine 1250mg/m^2	PO	twice daily from Day 1 to Day 14, followed by 7 days rest
	Mitomycin C 7mg/m^2	IV	**every 6 weeks**

Administration: Mitomycin C via fast running infusion of 0.9% Sodium Chloride
Capecitabine tablets should be swallowed with water within 30 minutes after a meal.

Frequency: 3 weekly cycle for 8 cycles **(N.B. Mitomycin C every 6 weeks x 4 doses)**

Main Toxicities: myelosuppression; diarrhoea; hand-foot syndrome (PPE); mucositis; haemolytic uraemic syndrome: cardiotoxicity (uncommon); ovarian failure/infertility

Anti- emetics: mildly emetogenic

Regular Investigations:	FBC	Day 1
	U&Es* & LFTs	Day 1 (*monitor renal function closely)
	CEA	Day 1
	ECG	If previous history of heart disease
	CT scan	Week 12 and Week 24

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.

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	Delay treatment for 1 week. Repeat FBC. If recovered, continue with full-dose MMC, and capecitabine with dose adjusted according to worst grade of haematological toxicity recorded - see table below (see Appendices for CTC grading)

Non-Haematological Toxicities: **Note that severe diarrhoea and/or severe mucositis early in the first treatment cycle can be the first presenting toxicity due to DPD enzyme deficiency, in which case potentially fatal neutropenia can quickly follow.**

Toxicity due to capecitabine may be managed symptomatically and/or modification of the dose (treatment interruption or dose reduction). Use the table below for dose adjustment guidelines. Once the dose has been reduced, it should not be increased at a later time. Doses of capecitabine omitted for toxicity are not replaced or restored. Instead the patient should resume the planned treatment cycle.

Haematological and Non-Haematological Dose Adjustment Guidelines according to Common Toxicity Criteria

Common Toxicity Criteria	During Course of Therapy	Dose adjustment for next cycle (% of start dose)
Grade 1	Maintain dose level	Maintain dose level
Grade 2: 1st Appearance	Interrupt until resolved to Grade 0 – 1	Give 100% dose
Grade 2: 2nd Appearance	Interrupt until resolved to Grade 0 – 1	Give 75% dose
Grade 2: 3rd Appearance	Interrupt until resolved to Grade 0 – 1	Give 50% dose
Grade 2: 4th Appearance	Discontinue treatment permanently	
Grade 3: 1st appearance	Interrupt until resolved to Grade 0 – 1	Give 75% dose
Grade 3: 2nd appearance	Interrupt until resolved to Grade 0 – 1	Give 50% dose
Grade 3: 3rd appearance	Discontinue treatment permanently	
Grade 4: 1st appearance	Discontinue permanently **or, with Consultant approval,** interrupt until resolved to Grade 0 – 1	Give 50% dose

Renal Impairment: Before every cycle, creatinine clearance should be calculated using Cockcroft and Gault. If borderline, an EDTA should be requested.

CrCl (ml/min)	Capecitabine Dose
> 50	Give 100% dose
30 – 50	Give 75% dose
< 30	Omit

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

Hepatic Impairment: If bilirubin > 3 x ULN **or** ALT/AST > 2.5 ULN, omit capecitabine until liver function recovers

Cardiotoxicity: Has been associated with fluoropyrimidine therapy (including myocardial infarction, angina, arrhythmias, cardiogenic shock, sudden death and ECG changes). Therefore, exercise caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.

References:
Rao, S et al, Br J Cancer, 2004; 91 (5): 839 -843
Jones, R et al; Annals of Oncology, Vol 13, 2002, Supplement 5, Abstract 312, page 86