CAPECITABINE

1. An option for metastatic colorectal cancer
2. Adjuvant use in Stage III or high risk Stage II colorectal cancer
3. An option for second-line use in advanced or metastatic pancreatic cancer

Drug/Dosage:	Capecitabine	1250mg/m^2	PO twice daily	from Day 1 to Day 14, followed by 7 days rest (i.e. 21 day cycle)

Administration: Tablets should be swallowed whole with water within 30 minutes after a meal.

Frequency: 3 weekly cycle, with clinical review prior to each cycle
Metastatic use: re-evaluate after 4 cycles
Adjuvant crc use: 8 cycles

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

Anti- emetics: mildly emetogenic

Regular Investigations:		
	FBC	Day 1
	U&Es*	Day 1 (*renal function should be closely monitored)
	LFTs	Day 1
	CEA	metastatic crc - every cycle adjuvant crc - every 6 – 8 weeks
	Ca 19-9	pancreas – every cycle
	ECG	if previous history of heart disease
	CT scan	after 4 cycles (advanced use only)

Dose Modifications

Haematological Toxicity:	Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l	Delay treatment for 1 week. Repeat FBC. If recovered, re-start capecitabine, using dose adjustment guidelines in table below, according to worst grade of haematological toxicity recorded.

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 may be requested.

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

Hepatic Impairment: 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:

Hoff, PM et al, JCO, April 2001; Vol 19, No 8: pp 2282 – 2292 (metastatic crc)
Van Custem et al, JCO, Vol 19 (21), 2001, pp 4097-4106 (metastatic crc)
Cassidy, J et al, JCO 2004, ASCO Annual Meeting Proceedings Vol 22, No 14S (July 15 Supplement): 3509 (adjuvant crc)
Twelves, C et al; NEJM 2005; 352 (26): 2696 – 2704 (adjuvant crc)
Cartwright, TH et al; JCO 2002; 20 (1): 160 – 164 (pancreas)