CAPECITABINE AND RADIOTHERAPY

For pre-operative use in rectal cancer, in patients whose disease needs down-staging
Concomitant chemo-radiotherapy for selected patients receiving radical radiotherapy for rectal cancer
For post-operative use in selected patients with rectal cancer

Drug/Dosage: Capecitabine 825mg/m^2 PO twice daily on Mondays to Fridays for 5 – 6 weeks

Radiotherapy: 45 - 54Gy in 25-30 fractions (1.8Gy/#) on weekdays only over the same 5 – 6 week period

Administration: Capecitabine and RT both administered 5 days per week (Mon – Fri) for 5 – 6 weeks.
Ideally, the first dose of capecitabine should be taken **at least** 1 to 2 hours before the first fraction of radiotherapy.
Capecitabine is available as 500mg and 150mg tablets, and should be swallowed with water within 30 minutes after a meal.
Note: Patients should be counselled to only take capecitabine on the days when radiotherapy is being given, and not on any other day.
i.e. number of days of capecitabine is equal to number of fractions of RT.

If capecitabine doses are omitted due to capecitabine-related toxicity, radiotherapy should continue. Once RT completed, capecitabine treatment should not continue.

Frequency: a single 5 - 6 week course
Clinic review for all patients routinely during week 3 and week 5
Other clinic appointments only as indicated on an individual basis

Main Toxicities: myelosuppression; diarrhoea; palmar-plantar erythema (PPE); mucositis; cardiotoxicity (uncommon); ovarian failure/infertility; impotence (males); urinary frequency/cystitis

Anti- emetics: mildly emetogenic

Regular Investigations:		
	FBC	baseline and during Week 3 & Week 5
	U&Es	baseline and during Week 3 & Week 5
	LFTs	baseline and during Week 3 & Week 5
	ECG	if previous history of angina, MI or rhythm disturbances

Dose Modifications

Haematological Toxicity:		
	Neutrophils < 1.0* x 10^9/l or Platelets < 80* x 10^9/l	Delay capecitabine for 1 week, but continue with RT. Repeat FBC. If recovered, restart capecitabine, using dose adjustment guidelines in table below, according to worst grade of haematological toxicity recorded.

*Increase FBC monitoring to at least weekly if counts borderline, but just above these levels.

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: Calculate creatinine clearance using Cockcroft and Gault. If borderline, an EDTA should be requested.

Creatinine Clearance (ml/min)	Capecitabine Dose
≥ 30	Give 100% 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:
Ngan, S et al, Proceedings ASCO 2001; 20; 591
Rich, T, Shepard, R and Mosley, S; JCO 2004; 22 (11): 2214 – 2232