

CAPECITABINE AND RADIOTHERAPY

An option in locally advanced non-metastatic cancer of the pancreas in patients with good performance status and who have not progressed on first-line chemotherapy

For post-operative use in selected patients with gastric cancer with a high risk for loco-regional failure

Drug/Dosage:	Capecitabine 830mg/m ² PO BD on Mondays to Fridays during RT (i.e. 5 or 5½ weeks)	
Radiotherapy:	Pancreas: 50.4Gy given as 28 fractions (1.8Gy/fraction) on Mondays to Fridays for 5½ weeks Gastric: 45 Gy given over 25 fractions (1.8Gy/fraction) on weekdays only for 5 weeks	
Other Drugs:	Ondansetron 8mg po once daily, one hour prior to radiotherapy Domperidone 10mg po three times daily as required Proton pump inhibitor at standard dose for 12 weeks from start of this regimen Loperamide as required for diarrhoea	
Administration:	Capecitabine and RT both administered 5 days per week (Mon – Fri) during radiotherapy. 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 course - 5½ weeks for pancreas; 5 weeks for gastric Review weekly	
Main Toxicities:	myelosuppression; diarrhoea; palmar-plantar erythema (PPE); mucositis; cardiotoxicity (uncommon); ovarian failure / infertility; GI haemorrhage or perforation – all patients require PPI cover for 12 weeks	
Anti- emetics:	Capecitabine: mildly emetic Radiotherapy: highly emetic (ondansetron 8mg po once daily, one hour prior to RT)	
Regular Investigations:	FBC	every week
	U&Es & LFTs	Day 1 and during Week 3 & Week 5
	ECG	if previous history of angina, MI or rhythm disturbances

Dose Modifications

Haematological Toxicity:	Neutrophils $\geq 1.0 \times 10^9/l$ or Platelets $> 100 \times 10^9/l$	Continue with treatment.
	Neutrophils $\geq 1.0 \times 10^9/l$ BUT Platelets 75 - $100 \times 10^9/l$	Give 75% dose of capecitabine for the next week. Once counts recovered, the dose may be increased to 100%. Continue with RT.

Reason for Update: gastric indication added	Approved by Consultant: Dr S Cummins
Version: 4	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 3	Date: 16.5.16
Prepared by: S Taylor	Checked by: C Tucker

Neutrophils 0.5 - 1.0 x 10 ⁹ /l or Platelets 50 - 75 x 10 ⁹ /l	Omit capecitabine for the next week. Once counts recovered, give 75% dose capecitabine. Continue with RT.
Neutrophils < 0.5 x 10 ⁹ /l or Platelets < 50 x 10 ⁹ /l	Omit RT and capecitabine. Recheck FBC in 3 days. RT may recommence once neuts > 0.5 and platelets > 50. Re-start capecitabine at 75% dose for all further treatment once neutrophils > 1.0 and platelets > 75.

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.

Dose Adjustment Guidelines for Diarrhoea or Nausea & Vomiting according to Common Toxicity Criteria

Common Toxicity Criteria	During Course of Therapy	Capecitabine dose adjustment once re-started (% of start dose)
Grade 1	Maintain dose level of capecitabine and RT.	Maintain dose level
Grade 2 despite full anti-emetics or anti-diarrhoeals	Interrupt capecitabine and radiotherapy until resolved to Grade 0 – 1.	Give 75% dose
Grade 3: 1 st appearance	Interrupt capecitabine and radiotherapy until resolved to Grade 0 – 1	Give 75% dose
Grade 3: 2 nd appearance	Discontinue CRT treatment permanently	-
Grade 4: 1 st appearance	Discontinue CRT treatment permanently	-

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 or angina.

References: Mukherjee, S et al; Lancet Oncol 2013; 14 (4): 317 - 326
Lee, J et al; JCO 2012; 30 (3) : 268 - 273

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