

CAPECITABINE with concurrent RT

INDICATION (ICD10) C20

1. Locally advanced rectal cancer neoadjuvant chemo-radiation. PS 0, 1, 2

REGIMEN

Days 1 to 5	CAPECITABINE	825mg/m ² (1650mg/m ² /day)	oral	twice daily
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Patients over 70 years (depending on PS) consider dose reduction

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every week for duration of radiotherapy ie 5 or 6 weeks in total

ANTI-EMETICS

Low risk days on days of capecitabine

CONCURRENT MEDICATION REQUIRED

Capecitabine	Mouth and bowel support eg_loperamide, benzydamine mouthwash
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ADMINISTRATION

Capecitabine	should be taken 12 hours apart. Swallowed with water within 30 minutes after a meal, or dissolve in 200ml luke warm water, stir thoroughly (squash may be added if unpalatable).
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EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs Neutrophils $\geq 1.5 \times 10^9/L$ Platelets $\geq 100 \times 10^9/L$	baseline and 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 TOXICITIES AND ADVERSE REACTIONS

Capecitabine	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function. To minimise risk of anthracycline induced cardiac failure signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. All patients should be told to report any cardiac symptoms immediately and should be told to stop the medication immediately if any suspicion of cardiac problems. Stomatitis
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INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Capecitabine	Brivudine and analogues should be avoided Warfarin and caution with all oral anticoagulants Phenytoin Allopurinol
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DOSE MODIFICATIONS

DPYD variant identified follow national or local DPD dose modification guidelines.

Haematological

Capecitabine

Grade	Toxicity	Radiotherapy - following a clinical review only	Capecitabine
1	Neutrophils <LLN- $1.5 \times 10^9/L$ Platelets <LLN- $75 \times 10^9/L$	Continue Continue	100% 100%
2	Neutrophils < $1.5-1.0 \times 10^9/L$ perform FBC x 2 per week Platelets < $75-50 \times 10^9/L$ perform FBC x 2 per week	Continue Interrupt until grade 0-1	100% Interrupt until grade 0-1 then 100%
3	Neutrophils < $1.0-0.5 \times 10^9/L$ perform FBC daily Platelets < $50-25 \times 10^9/L$ perform FBC daily Neutropenic sepsis with grade 3 or 4 diarrhoea	Continue Interrupt until grade 0-1. Interrupt until grade 0-1 and $\leq 6mg$ loperamide/24 hours required and patient fit.	Interrupt until grade 0-1 then 75% Interrupt until grade 0-1 then 75% permanently
4	Neutrophils < $0.5 \times 10^9/L$ perform FBC daily Platelets < $25 \times 10^9/L$ perform FBC daily	Interupt until grade 0–1 and patient fit Interupt until grade 0–1 and patient fit	Stop permanently Stop permanently

In the event of a second grade 3 episode of the same toxicity, treatment should discontinue permanently.

Non-haematological

Capecitabine

Diarrhoea

Grade	Toxicity	Radiotherapy - following a clinical review only	Capecitabine
1	Increase <4 stools per day over baseline, mild increase in ostomy output	Continue	100%
2	Increase 4-6 stools per day over baseline, mild increase in ostomy output. Moderate cramping (>12 hours or <12 hours)	<12hours duration – continue >12hours duration – Interrupt until grade 0-1 then resume	Omit evening dose at onset, reassess 24 hours later. If <12 hours duration continue. Interrupt until grade 0-1 then 75%.
3	Increase ≥7 stools per day over baseline, severe increase in ostomy output. Severe cramping or peritonism	Interrupt until grade 0-1	Interrupt until grade 0-1 then 75%. If neutropenic sepsis stop permanently
4	Life threatening consequences urgent intervention indicated	Stop permanently	Stop permanently

Mucositis

Grade	Radiotherapy following clinical review	Capecitabine
1	Continue	100%
2	Continue	Interrupt until grade 0-1 then give 75%
3	Continue but treat with appropriate supportive therapy	Interrupt until grade 0-1 then give 75%
4	Continue but treat with appropriate supportive therapy	Stop permanently

Skin

Grade	Toxicity	Capecitabine
1	Minimal skin changes or dermatitis (eg erythema, oedema, or hyperkeratosis) without pain	Continue
2	Skin changes (eg peeling, blisters, bleeding, oedema or keratosis) with pain limiting instrumental ADL	Interrupt until 0-1 then resume at 75%
3	Skin changes (eg peeling, blisters, bleeding, oedema or keratosis) with pain limiting instrumental ADL	Interrupt until 0-1 then resume at 75%

In the event of a second grade 3 episode of the same toxicity, treatment should discontinue permanently.

Hepatic impairment

Capecitabine

Grade 2 bilirubin of >1.5-3xULN perform blood tests x2 per week	Give 75%
Grade 3 bilirubin of >3-10xULN	Stop permanently
Grade ≥2 ALT/AST >3xULN perform blood tests x2 per week	Interrupt until grade 0–1, restart at 75% dose

Renal impairment

Capecitabine

CrCl >50ml/min	give 100% dose
CrCl 30-50ml/min	give 75% dose
CrCl <30ml/min	contraindicated

REFERENCES

1. Yu CS et al. Optimal time interval between capecitabine intake and radiotherapy in preoperative chemoradiation for locally advanced rectal cancer. *Int J Radiat Oncol Biol Phys* 2007; 67 (4): 1020-1026.
2. Saif MW et al. Capecitabine vs continuous infusion 5-FU in neoadjuvant treatment of rectal cancer. A retrospective review. *Int J Colorectal Dis* 2008; 23 (2): 139-145.
3. Lim HJ et al. A comparison of capecitabine versus infusional 5-FU used concurrently with preoperative radiation for rectal cancer: a population based study. *Am Soc Clin Oncol Gastrointestinal Cancers Symposium* 2008; Abstract 477.
4. Aristotle study version 2.0 December 2011

Assessments

	Pre	Week 1	Week 2	Week 3	Week 4	Ongoing	Last cycle
Clinical assessment	X					At the start of the cycle	
SACT assessment (PS and toxicities)	X	X	X	X	X	Every week	Check has OPD
FBC	X	X	X	X	X	Every week	X
U&E, calcium, & LFT	X	X	X	X	X	Every week	X
CrCl	X	X	X	X	X	Every week	X
Dihydropyrimidine dehydrogenase (DPYD) deficiency test	X					This test is required for every patient newly started on capecitabine or fluorouracil. The result MUST be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary.	
CT scan	X					Clinician to book	Check has date for CT
Informed consent	X					Verbal each cycle	
Height	X					Every cycle	
Weight recorded	X	X	X	X	X	Every week	X