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 900mg/m^2 twice daily (1800mg/m^2/day) oral followed by 2 day rest

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

ADMINISTRATION
Tablets 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).

ANTI-EMETICS
Low risk days on days of capecitabine

CONCURRENT MEDICATION REQUIRED

Capecitabine	Mouth and bowel support eg Loperamide, benzydamine mouthwash

EXTRAVASATION AND TYPE OF LINE / FILTERS
Not applicable

INVESTIGATIONS
Blood results required before SACT administration
FBC, U&E and LFTs every week
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Serum creatinine - GFR each cycle
DPD test
Baseline weight and every cycle

MAIN TOXICITES 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

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

DOSE MODIFICATIONS
Haematological

Grade	Toxicity	Radiotherapy - following a Clinicial review only	Capecitabine
1	Neutrophils <LLN-1.5x10^9/L Platelets <LLN-75x10^9/L	Continue Continue	100% 100%
2	Neutrophils <1.5-1.0x10^9/L perform FBC x 2 per week Platelets <75-50x10^9/L perform FBC x 2 per week	Continue Interrupt until grade 0-1	100% Interrupt until grade 0-1 then 100%
3	Neutrophils <1.0-0.5x10^9/L perform FBC daily Platelets <50-25x10^9/L perform FBC daily Neutropenic sepsis with grade 3 or 4 diarrhoea	Continue Interrupt until grade 0-1 Interrupt until grade 0-1 and ≤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 <0.5x10^9/L perform FBC daily Platelets <25x10^9/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
Diarrhoea

Grade	Toxicity	Radiotherapy - following a Clinicial 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 hrs 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 Clinicial 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 (ml/min) >50	give 100% dose
CrCl (ml/min) 30-50	give 75% dose
CrCl (ml/min) <30	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