Systemic Anti Cancer Treatment Protocol

Capecitabine Chemoradiation

PROTOCOL REF: MPHACAXRT
(Version No: 1.1)

Approved for use in:

Rectal cancer in combination with radiotherapy

Dosage:

Drug	Dosage	Route	Frequency
Capecitabine	825mg/m^2 BD	PO	Twice daily (morning and evening) on radiotherapy days for 25 days

Course length may be increased to 28 days

Caution in patients with pre-existing coronary heart disease, angina pectoris, arrhythmias or chronic anticoagulant or high dose aspirin use.

See renal dose adjustments table below.

Do not start capecitabine if baseline ANC<1.0 x 10^9/L OR platelets < 100 x 10^9/L

Supportive treatments:

Anti-emetic Risk - Low

Loperamide 4mg immediately after first liquid stool followed by 2mg every 2 hours for at least 12 hours

Domperidone 10mg oral tablets, up to 3 times a day or as required

Administration:

Tablets are available in 150mg and 500mg strengths.

Counselling points:

Tablets should be taken 12 hours apart, morning and evening on days of radiotherapy only (Monday to Friday).

Swallow whole with water within 30 minutes of a meal.

Do not add doses missed due to toxicity onto the end of the cycle. Continue according to the treatment plan and stop taking on the originally scheduled day.

Take missed doses if remembered within 2 hours of the normal scheduled time. Otherwise continue with the next scheduled dose. Do not double up missed doses.

In case of swallowing difficulties the tablets may be dissolved in 200ml warm water. Once dissolved stir the contents with a spoon and drink immediately. Wash well and reserve the glass and spoon for chemotherapy administration only.

Drug Interactions

Allopurinol – reduced efficacy of capecitabine – avoid
Clozapine – additive risk of agranulocytosis
Folic acid – increased risk of side effects of capecitabine, avoid if possible – discuss with pharmacy
Phenytoin – potentially toxic levels of phenytoin have been reported- monitor carefully
Warfarin and other coumarin anticoagulants – increased bleeding risk, monitor INR carefully, consider switch to LMWH

Main Toxicities:

Myelosuppression, diarrhoea, Palmar Plantar Erythema (PPE or hand- foot syndrome), stomatitis, fatigue, asthenia, anorexia, cardiotoxicity (uncommon), ovarian failure/infertility, increased renal dysfunction on those with preexisting compromised renal function, and thrombosis/embolism

DPD deficiency – leads to severe early fluorouracil toxicity, affects approximately 3% of population, may be life threatening

Investigations and Treatment Plan

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X		X		X	Alternate cycles
Nursing Assessment	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
Dihydropyrimidine dehydrogenase (DPD) deficiency test	X					This test is normally only required if a patient has not had capecitabine, or fluorouracil in the past. However a consultant may still request this test if capecitabine or fluorouracil was not tolerated previously. The result must be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary. Treatment with capecitabine and fluorouracil is contraindicated in patients with known complete DPD deficiency.
CT scan	X					
Informed Consent	X					
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Non-haematological toxicities

If patients experience toxicities in general manage toxicities symptomatically and/or with dose modification. Withhold treatment until toxicities have resolved to grade 1. Do not increase doses of capecitabine once they have been reduced.

<table>
<tr><th>Toxicity</th><th>Management</th></tr>
<tr><td>Renal</td><td>Calculate CrCl using Cockroft and Gault formula at baseline and at week 3 and adjust dose according to table
<table>
<tr><th>CrCl (ml/min)</th><th>Capecitabine dose</th></tr>
<tr><td>>50</td><td>Give 100% dose</td></tr>
<tr><td>30-49</td><td>Give 75% dose</td></tr>
<tr><td>< 30</td><td>Omit</td></tr>
</table></td></tr>
<tr><td>Hepatic</td><td>
<table>
<tr><th>Toxicity</th><th>Management</th></tr>
<tr><td>Bilirubin > 3 x ULN or ALT/AST > 2 x ULN</td><td>Omit capecitabine until liver function recovers</td></tr>
</table></td></tr>
<tr><td>Diarrhoea</td><td>Loperamide at standard doses – ensure maximum dose reached, codeine may be added – see table below for dose reductions</td></tr>
<tr><td>Stomatitis</td><td>Regular mouthwashes (water, saline or non alcoholic proprietary brand), brush gently with a soft brush, adequate pain relief, nutritional support in severe cases – see below for dose reductions.</td></tr>
<tr><td>Palmar plantar erythema or hand foot syndrome</td><td>Manage as per trust policy, withhold treatment until resolved to grade 1, dose reductions as per table below.</td></tr>
<tr><td>Sore eyes / Conjunctivitis</td><td>Eye drops for symptomatic treatment such as hypromellose 0.3% – avoid antimicrobial eyedrops unless indicated for infective conjunctivitis</td></tr>
<tr><td>Chest Pain / coronary artery spasm</td><td>Stop capecitabine, standard angina investigations, refer to consultant, if symptoms persist stop capecitabine permanently</td></tr>
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Cockroft and Gault formula

Male patients $\frac{1.23 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Female patients $\frac{1.04 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Haematological and Non-haematological dose adjustment guidelines according to Common Toxicity Criteria

Toxicity grades / Haematological parameter	**Dose changes within a treatment cycle**	**Dose adjustment for next cycle/dose** **(% of starting dose)**
• Grade 1	Maintain dose level	Maintain dose level
• Grade 2		
-1st appearance	Interrupt until resolved to grade 0-1	100%
-2nd appearance		75%
-3rd appearance		50%
-4th appearance	Discontinue treatment permanently	Not applicable
• Grade 3		
-1st appearance	Interrupt until resolved to grade 0-1	75%
-2nd appearance		50%
-3rd appearance	Discontinue treatment permanently	Not applicable
• Grade 4		
-1st appearance	Discontinue permanently Or If physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1	50%
-2nd appearance	Discontinue permanently	Not applicable

References:

Summary of Product Characteristics Xeloda© Electronic Medicines Compendium accessed on 28/02/2017 at 21.42 https://www.medicines.org.uk/emc/medicine/4619

British National Formulary accessed on 28/02/2017 at 21.43 on https://www.evidence.nhs.uk/formulary/bnf/current

Twelves, C et al; NEJM 2005; 352 (26): 2696 – 2704 (adjuvant crc)