Systemic Anti Cancer Treatment Protocol

Capecitabine Breast Cancer

PROTOCOL REF: MPHACAPEBR
(Version No: 1.2)

The protocol has been temporarily amended – please see the Oral SACT Operational Changes during Covid-19. Amendments may include less frequent blood monitoring, telephone SACT assessments and longer durations of treatment being dispensed.

Approved for use in:

Locally advanced and/or metastatic breast cancer

Dosage:

Drug	Dosage	Route	Frequency
Capecitabine	850mg/m^2 Or 1000mg/m^2 Or 1250mg/m^2	PO	Twice daily (morning and evening) for 14 days

Start at a maximum dose of 1000mg/m^2 for patients over 70 years or PS 2

Repeat every 21 days for 6 cycles and reassess, continue subject to patient choice, tolerability and response

Caution in patients with pre-existing coronary heart disease, angina pectoris, arrhythmias or those on high dose aspirin or anticoagulants

Supportive treatments:

Anti-emetic Risk - Low

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

Loperamide 2mg after each loose stool

Ensure patients are counselled to regularly moisturise hands and feet

Extravasation risk:

Not applicable

Administration:

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

Notes

Tablets should be taken 12 hours apart.

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

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.

Sorivudine and analogues – Potentially fatal interaction – avoid completely

Allopurinol – reduced efficacy of capecitabine – avoid.

Main Toxicities:

Haematological	Neutropenia, anaemia, thrombocytopenia,
Cardiac and Vascular disorders	Angina
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, mucositis
Hepatobiliary	Elevation of liver transaminases, alkaline phosphatase and bilirubin.
Skin and subcutaneous tissue disorders	Palmar Plantar Erythema (PPE or hand- foot syndrome),
General disorders and administration site conditions	Fatigue, taste changes Infertility, early menopause

DPD deficiency – leads to severe early 5FU toxicity, affects approximately 3-6% of population, may be life threatening in up to 1% of cases.

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	Every cycle
FBC	X		X	X	X	Every cycle
U&E & LFT	X		X	X	X	Every cycle
CrCl (Cockroft and Gault formula)	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					As clinically indicated
Informed Consent	X					
ECG*	X					Repeat as clinically indicated
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X		X	X	X	
Weight recorded	X	X	X	X	X	Every cycle
Height recorded	X					

*If previous history of heart disease

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if all apply:-

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

Delay 1 week on day 1 if any apply:-

ANC ≤ 0.9 x 10^9/L	Platelets ≤ 99 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 before each cycle 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 to 50</td><td>Give 75% dose</td></tr>
<tr><td>< 30</td><td>Omit</td></tr>
</table></td></tr>
<tr><td>Hepatic</td><td>Not studied in severe hepatic impairment.
No dose adjustment is needed</td></tr>
<tr><td>Diarrhoea</td><td>Loperamide at standard doses, codeine may be added – see table below for dose reductions</td></tr>
<tr><td>Stomatitis</td><td>Regular mouthwashes (water, saline), 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>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</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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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:

Blum JL et al, JCO 1999 17(2):485

Henricks LM, Lunenburg CA, de Man FM et al. DPYD genotype-guided dose individualisation of fluoropyrimidine therapy in patients with cancer: a prospective safety analysis. Lancet Oncol 2018; 19: 1459–67

NICE TA62 2003, now updated in CB81 August 2017

O'Shaughnessy JA et al, Annals of Oncology 2001 12:1247-1254

Supplement to: Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; **20:** e201–08.