Systemic Anti Cancer Treatment Protocol

Fluorouracil and Folinic Acid (Chemoradiation weekly or infusion)

PROTOCOL REF: MPHAFFXRTGA
(Version No: 1.1)

Approved for use in

With radiotherapy for rectal cancer - chemoradiation

Dosage:

Weekly

Drug	Dosage	Route	Frequency
Folinic Acid	50mg	IV	Weekly
Fluorouracil	300mg/m^2	IV	Weekly

OR

Infusion

Drug	Dosage	Route	Frequency
Fluorouracil	1000mg/m^2	IVI	Day 1 to 4
Fluorouracil	1000mg/m^2	IVI	Day 22 to 26

Supportive treatments:

Antiemetic risk - low

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

Loperamide 4mg initially then 2mg after each loose stool

Extravasation risk:

Network guidelines suggest that fluorouracil is an irritant and should be treated as such using Network guidance.

PICC lines are usually inserted for patients undergoing infusional fluorouracil at home

Administration:

Weekly

Day	Drug	Dosage	Route	Frequency	Diluent and rate
1	Folinic Acid	50mg	IV	Once weekly for 5 weeks	IV bolus
1	Fluorouracil	300mg/m^2	IV	Once weekly for 5 weeks	IV bolus

OR

Infusion

Day	Drug	Dosage	Route	Frequency	Diluent and rate
1 to 4	Fluorouracil	1000mg/m^2	IV	Daily over 24 hours for four days	IV infusion
22 to 26	Fluorouracil	1000mg/m^2	IV	Daily over 24 hours for four days	IV infusion

Administration notes:

Administer Calcium Folinate before fluorouracil for weekly administration.

Administer chemotherapy prior to radiotherapy.

Caution in patients with pre-existing heart disease, angina pectoris, arrhythmias.

Adverse effects of either chemotherapy or radiotherapy may be potentiated with combined treatment.

Sorivudine and analogues – **Potentially fatal interaction** – avoid completely.

Medical/Nursing review as per patient management plan

For severe reactions, discuss with Consultant before continuing with treatment.

Main Toxicities:

Diarrhoea, nausea and vomiting, conjunctivitis / sore eyes, skin rashes, Palmar Plantar Erythema (PPE or hand foot syndrome), stomatitis, chest pain (myocardial ischaemia or angina), ovarian failure / infertility, nail ridges, taste changes

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

Investigations and treatment plan:

	Pre	Week 1	Week 2	Week 3	Week 4	Week 5	Ongoing
Medical / Senior nurse / AHP Assessment		x	x	x	x	x	
Nursing Assessment		x					
FBC weekly	x	x			x		Or if clinically indicated
FBC infusion	x	x				x	Or if clinically indicated
U&E & LFT weekly	x	x	x	x	x	x	If clinically indicated
U&E & LFT infusion	x	x				x	
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						Arranged by surgical team following treatment
Informed Consent	x						
Blood pressure measurement	x						
PS recorded	x	x			x	x	
Toxicities documented	x	x	x	x	x	x	
Weight recorded	x	x				x	Pre chemotherapy
Urine dipstick for protein	x						If clinically indicated

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

Inform team and delay 1 week on day 1 if any apply:-

ANC <1.0 x 109/L	Platelets < 100 x 10^9/L

If platelets or ANC still below required levels for treatment at week 2, refer to consultant oncologist for advice regarding any toxicity ≥ grade 2

Recommended dose reduction	**Fluorouracil**
Grade 2	Reduce all subsequent doses of fluorouracil by 20%
Grade 3	Discontinue chemotherapy; consider interruption in radiotherapy.
Grade 4	Discontinue treatment

Non-haematological toxicities

Following assessment treatment should be withheld for any toxicity until resolved to grade 1

Toxicity	Management
Renal	Dose reduction only needed for severe renal impairment CrCl < 30ml/min give 75% dose
Hepatic	Treatment at physician discretion. If bilirubin > 85 or AST > 180 consider reducing starting dose by 1/3 to ½ depending on severity. Doses can be increased if no toxicity seen
Chest pain, coronary artery spasm	Stop fluorouracil, standard angina investigations, refer to consultant, if symptoms persist stop permanently
Stomatitis	If mouth ulcers or > grade 2 symptoms develop treat symptomatically as per UKONS guide Delay treatment until resolved to grade 1 and reduce fluorouracil doses by 20%. See table

<table>
<tr><td>Diarrhoea</td><td>Monitor increase of bowel/stoma output over pre-treatment normal. Treat diarrhoea between cycles symptomatically. Commence regimen specific antidiarrhoeal as indicated
If diarrhoea has not resolved by next cycle delay treatment by 1 week.
If diarrhoea persists or more than 1 delay is required reduce both fluorouracil bolus and infusion doses by 20% and continue at the lower dose unless further toxicity occurs - See table
<table>
<tr><th>Grade 0</th><th>Grade 1</th><th>Grade 2</th><th>Grade 3</th><th>Grade 4</th></tr>
<tr><td>None or no change from normal</td><td>Increase of up to 3 bowel movements a day over pre-treatment normal or mild increase in ostomy output</td><td>Increase of up to 4-6 episodes a day or moderate increase in ostomy output or nocturnal movement or moderate cramping</td><td>Increase of up to 7-9 episodes a day or severe increase in ostomy output or incontinence / severe cramping / bloody diarrhoea</td><td>Increase >10 episodes a day or grossly bloody diarrhoea</td></tr>
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<tr><td>PPE</td><td>Treat symptomatically, delay treatment until resolved to grade 1. Reduce fluorouracil doses (bolus and infusion) by 20% for subsequent doses if persistent troublesome PPE. See table</td></tr>
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Dose reductions for non haematological toxicities

	Non haematological toxicities (diarrhoea and stomatitis) As below or consultant discretion			
grade	0-1	2	3	4
1st occurrence	100%	100%	60%	Stop treatment
2nd occurrence	80%	80%	50%	Stop treatment
3rd occurrence	60%	60%	50%	Stop treatment

References:

https://www.nwcscnsenate.nhs.uk/files/2514/1820/9753/CMSCN_NETWORK_GUIDANCE_FOR_THE_PREVENTION_AND_MANAGEMENT_OF_EXTRAVASATION_INJURIES_V._5.0_Jan_2014.pdf

Comparison of fluorouracil with additional levamisole, higher dose folinic acid or both as adjuvant chemotherapy for colorectal cancer a randomised trial. QUASAR Collaborative Group. Lancet 2000; 355 (9215): 1588-1569

Kerr et al, Adjuvant chemotherapy with 5-fluorouracil, L-folinic acid and levamisole for patents with colorectal cancer: Non randomised comparison of weekly versus four weekly schedules – less pain same gain. Annals of Oncology 2000; 11(8):947-955

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Roh et al, Preoperative multimodality therapy improves disease free survival in patients with carcinoma of the rectum NSABP R-03. J Clin Oncol. 2009; 27(31):5124