Systemic Anti Cancer Treatment Protocol

Fluorouracil and Folinic Acid (Weekly)

PROTOCOL REF: MPHAFLFAGA
(Version No: 1.2)

This protocol has been temporarily amended - please see the SRG Guidelines during COVID-19 Lower GI cancer

Approved for use in:

Adjuvant colorectal cancer

Dosage:

Drug	Dosage	Route	Frequency
Folinic Acid	50mg	IV	Weekly for 24 weeks
Fluorouracil	370mg/m^2	IV	Weekly for 24 weeks

Supportive treatments:

Antiemetic risk - low

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

Loperamide 2mg after each loose stool

Extravasation risk:

Fluorouracil is IRRITANT and should be treated using Network guidance

Administration:

Day	Drug	Dosage	Route	Diluent and rate
1	Folinic Acid	50mg	IV	IV bolus over 3 to 5 minutes
1	Fluorouracil	370mg/m^2	IV	IV bolus over 3 to 5 minutes

Notes:

Administer folinic acid before fluorouracil

Sorivudine and analogues – Potentially fatal interaction – avoid completely

Care with patients on coumarin anticoagulants – monitor INR closely, consider LMWH

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	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing	Last cycle
Medical / NC / ANP Assessment	X					Mid way/end of treatment or as directed	Check has opd
Nursing Assessment	X	X	X	X	X	Every cycle	X
FBC	X				X	Every 4 weeks	X
U&E & LFT	X				X	Every 4 weeks	X
CrCl	X				X	Every 4 weeks	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					Per surgical surveillance	
Informed Consent	X					Confirmation at pre-assessment	
PS recorded	X	X	X	X	X	Every cycle	X
Toxicities documented	X	X	X	X	X	Every cycle	X
Weight recorded	X	X	X	X	X	Every cycle	X

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 10^9/L	Platelets <100 x 10^9/L

If platelets or ANC still below required levels for treatment at week 2, delay treatment again and patient will need assessment and chemotherapy dose reduction of 20%

NB. Bloods will need to be done weekly in this instance.

Non-haematological toxicity

Fluorouracil	
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 dose by 20%. See table
Diarrhoea	Monitor increase of bowel/stoma output over pre-treatment normal (guide below).Treat diarrhoea between cycles symptomatically. Commence regimen specific anti-diarrhoeal If diarrhoea has not resolved by next cycle - delay treatment by 1 week. If diarrhoea persists or more than 1 delay is required reduce fluorouracil bolus by 20% and continue at the lower dose unless further toxicity occurs
PPE	Treat symptomatically, delay treatment until resolved to grade 1. Reduce fluorouracil dose by 20% for subsequent doses if persistent troublesome PPE. See table

Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
None or no change from normal	Increase of up to 3 bowel movements a day over pre-treatment normal or mild increase in ostomy output	Increase of up to 4-6 episodes a day or moderate increase in ostomy output or nocturnal movement or moderate cramping	Increase of up to 7-9 episodes a day or severe increase in ostomy output or incontinence / severe cramping / bloody diarrhoea	Increase >10 episodes a day or grossly bloody diarrhoea

Fluorouracil dose reductions for non haematological toxicity

	Non haematological toxicities (diarrhoea, stomatitis, PPE) As below or consultant discretion			
grade	0-1	2	3	4
1st occurrence	100%	80%	80%	Stop treatment
2nd occurrence	80%	70%	60%	Stop treatment
3rd occurrence	60%	60%	50%	Stop treatment

References:

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

Kerr DJ, Gray R, McConkey C, et al. Adjuvant chemotherapy with 5-fluorouracil, L-folinic acid and levamisole for patients with colorectal cancer: non-randomised comparison of weekly versus four-weekly schedules--less pain, same gain. QUASAR Colorectal Cancer Study Group. *Annals of Oncology* 2000; 11(8):947-955