Systemic Anti Cancer Treatment Protocol

Modified De Gramont

PROTOCOL REF: MPHAMDGGA
(Version No: 1.0)

Approved for use in:

Advanced colorectal cancer

Dosage:

Drug	Dosage	Route	Frequency
Folinic Acid	350mg	IV	Every 14 days
Fluorouracil	400mg/m^2	IV	Every 14 days
Fluorouracil	2800mg/m^2	IV	Every 14 days

Advanced – give for 6 cycles and review, continue subject to patient choice, tolerability and response

Fluorouracil dose can be reduced to 2400mg/m^2 in patients with poorer performance status

Supportive treatments:

Anti-emetic 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:

PICC line will be usually inserted. Network guidelines suggest that fluorouracil is an IRRITANT and should be treated using Network guidance

Administration:

Day	Drug	Dosage	Route	Diluent and Rate
1	**Dexamethasone** 30 mins before chemotherapy	8mg	PO	
1	**Folinic Acid**	350mg	IV	250mL Glucose 5% infusion over 2 hours
1	**Fluorouracil**	400mg/m^2	IV	Bolus over 5 minutes
1 to 2	**Fluorouracil**	2800mg/m^2	IV	46 hour continuous infusion in Sodium Chloride 0.9%

Advanced – reassess after 6 cycles, continue subject to patient choice, tolerability and response

Notes:

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

Sorivudine and analogues – Potentially fatal interaction – avoid completely

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 / Senior Nurse / AHP Assessment	X		X		X	Alternate cycles or team discretion	
Nursing Assessment	X	X	X	X	X	Every cycle	Check has OPD
FBC	X	X	X	X	X	Every cycle	X
U&E & LFT	X	X	X	X	X	Every cycle	X
CrCl	X	X	X	X	X	Every cycle	X
CT scan	X					Inform consultant team if not booked	Check has date for CT
Informed Consent	X					Verbal each cycle	
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	

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 75 x 10^9/L

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

ANC <1.0 x 10^9/L	Platelets < 75 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 as follows.

Non-haematological toxicity

<table>
<tr><td>Renal</td><td>Calculate CrCl using Cockroft and Gault before each cycle.

<table><tr><th>Creatinine Clearance (mL/min)</th><th>Fluorouracil dose</th></tr><tr><td>≥ 30</td><td>Full dose</td></tr><tr><td>< 30</td><td>75%</td></tr></table>If moderate impairment monitor closely</td></tr>
<tr><td>Hepatic</td><td><table><tr><th>Liver function</th><th>Fluorouracil dose</th></tr><tr><td>Bilirubin > 85micromol/L</td><td>Omit</td></tr></table>
Note that significantly impaired hepatic function might be a sign of disease progression and require cessation or change of treatment.
Always discuss deteriorating organ function with consultant</td></tr>
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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. Treat diarrhoea between cycles symptomatically as per UKONS guide. 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

	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
PPE	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				

Fluorouracil dose reductions for non haematological toxicity

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

References:

Cheshire and Merseyside Strategic Clinical Networks. Network Guidance for the prevention and management of extravasation injuries V6.0 accessed 11.49 on 26/01/2017 on http://nww.clatterbridgecc.nhs.uk/application/files/5814/5934/5142/Prevention__Management_of_Extravasation_Injuries_V6.0.pdf

Summary of Product Characteristics, Electronic Medicines Compendium, fluorouracil 50mg/ml accessed on 26/01/2017 at 12.02 at http://www.medicines.org.uk/emc/medicine/636

de Gramont A, Bosset JF, Milan C, Rougier P, Bouche O, Etienne PL, et al. Randomized trial comparing monthly low-dose leucovorin and fluorouracil bolus with bimonthly high-dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 1997 15(2): 808-15