NHS
North West Coast
Strategic Clinical Networks

Chemotherapy protocol

Drug regimen
Modified de Gramont

Indications for use
Metastatic colorectal cancer

Regimen

Drug	Fluid	Time
Folinic Acid 350mg	250mls Glucose 5%	2 hours
5-Fluorouracil 400mg/m²		IV bolus
5 Fluorouracil 2400mg/m²		46 hours in infusor pump

Regimen to be repeated every 2 weeks for 6-12 cycles

Investigation prior to initiating treatment
FBC
LFTs
U&Es
Bone
CT scan
CEA

Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism (this can present as severe diarrhoea and/or severe stomatitis early in the first cycle). Patients require DPD testing prior to administration. Dose adjustments should be made in accordance with local DPD policy.

Investigations and consultations prior to each cycle
FBC, U&Es, LFTs every cycle
CEA and calcium every 2nd cycle

The liver function test may be retrospectively looked at (i.e. after the chemotherapy treatment) **unless** they are known to be abnormal then they need to be repeated the day before so that the results are available pre-chemotherapy.

Consultation every 4 weeks

Acceptable levels for treatment to proceed
(if outside these delay one week or contact consultant)
Acceptable blood range: Neutrophils $\geq 1.2 \times 10^9$/l and platelets $\geq 100 \times 10^9$/l

If only Hb is low (below 95g/dl) please contact doctor to arrange for blood transfusion but continue with chemotherapy

Side Effects
Sore mouth, conjunctivitis, skin rashes, nausea and vomiting, diarrhoea, hand foot syndrome, myelosuppression and thrombocytopenia, cardiotoxicity (including coronary artery spasm, angina and tachycardia), ocular toxicity (excessive lacrimation, visual change, photophobia), transient cerebellar syndrome, confusion, thrombophlebitis

Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism- avoid use in patients with known DPD deficiency

Dose Modification Criteria

Renal impairment

Consider dose reduction of fluorouracil if CrCl <10 ml/min (no dose adjustment needed for folinic acid)

Hepatic impairment

ALT	Fluorouracil dose	Folinic acid dose
<1.5 x ULN	100%	100%
1.5-3 x ULN	66% *	100%
3-5 x ULN	50% *	100%
>5 x ULN	Contraindicated	

*doses may be increased back to 100% if no toxicity

Other dose modifications should be made as per the following table

Toxicity grade	1st occurrence	2nd occurrence	3rd occurrence	4th occurrence
0-1	100%	100%	100%	100%
2	Delay then 100%	Delay then 75%	Delay then 50%	Discontinue
3	Delay then 75%	Delay then 50%	Discontinue	
4	Delay then 50%	Discontinue		

Delay until toxicity grade 0-1

Patients presenting with diarrhoea must be carefully monitored until the symptoms have disappeared as a rapid deterioration can occur

Specific Information to Administration
Treatment needs to be administered via a central line
Patients need assessing or a PICC prior to commencement of treatment
Administer folinic acid prior to 5FU

Patients should be informed of the need to interrupt treatment immediately if they develop moderate or severe side effects, particularly diarrhoea (not controlled by loperamide), palmar plantar erythrodyaesthesia, chest pain or infection.

THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON, CLINICIAN FOR COLORECTAL CANCER
RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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