North West Coast
Strategic Clinical Networks

Chemotherapy protocol

Drug regimen
Oxaliplatin and modified de Gramont

Indications for use

1.) Metastatic colorectal cancer with resectable or potentially resectable liver metastases
2.) Metastatic colorectal cancer

Regimen

DRUG	FLUID	TIME	
Oxaliplatin 85mg/m²	500mls 5% Glucose	2 hours	Administered concurrently
Folinic Acid 350mg	250mls 5% glucose	2 hours	
5-Fluorouracil 400mg/m²		IV bolus	
5-Fluorouracil 2400 mg/m		46 hours in infusor pump	

Regimen to be repeated every 2 weeks until disease progression

Investigation prior to initiating treatment
FBC
U&Es
LFT
Bone
CEA
Creatinine clearance
MR liver (with Primovist)/PET –CT scan if being considered for liver surgery

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.

Caution
Oxaliplatin should always be administered before fluoropyrimidines
Avoid cold drinks for 2-3 days after oxaliplatin infusion

Investigations and consultations prior to each cycle
FBC, U&Es, LFTs, calcium and magnesium every cycle
CEA every 4 weeks

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 4-6 weeks

Side Effects
Tiredness, diarrhoea and abdominal pain, nausea and vomiting, sore mouth, poor appetite, myelosuppression and thrombocytopenia, hand foot syndrome, cardiotoxicity (including coronary artery spasm, angina and tachycardia), ocular toxicity (excessive lacrimation, visual change, photophobia), peripheral neuropathy, cold related dysaesthesia (hands/feet or laryngopharyngeal), infusion reactions, pulmonary fibrosis, veno-occlusive disease, high tone and hearing loss, ovarian

failure/infertility, 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

Acceptable levels for treatment to proceed (if outside these delay one week or contact consultant)
Acceptable blood range: Neutrophils $\geq 1.5 \times 10^9$/l, platelets $\geq 100 \times 10^9$/l , Hb $\geq$ 95 g/l
If Neutrophils 1.2 – 1.5 $\times 10^9$/l contact **consultant**

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

Bil <3 x ULN
ALT/ALP <2.5 x ULN
Creatinine Clearance >30ml/min

If U&E abnormal check with consultant

Dose Modification Criteria

Renal impairment

Creatinine Clearance (ml/min)	5FU dose	Oxaliplatin dose
>50	100%	100%
30-50	100%	100%
<30	80%	Omit

Hepatic impairment

Bilirubin >3 xULN or ALT >2.5 ULN: Give 50% 5FU and Oxaliplatin until liver function recovers

Haematological toxicity

Grade I/II ANC No dose reduction
Grade III/IV Delay until recovered then proceed with 20% Oxaliplatin and 5FU reduction
If delay >1 week reduce 5FU and oxaliplatin dose by 20%.

Continue at reduced dose for subsequent cycles unless other toxicity occurs

If further delays for bone marrow suppression occur despite a 20% dose reduction consider further 20% dose reduction

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		

In grade 3 or 4 stomatitis or diarrhoea reduce Oxaliplatin dose to 65 mg/m^2

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

Any delays should be until toxicity has resolved to grade 0-1
Cumulative dose related peripheral sensory neuropathy

Usually occurs after a cumulative dose of 800mg/m^2, and can occur after oxaliplatin has completed

Grade1 (any duration) or grade 2 longer than 7 days	Continue oxaliplatin 85mg/m^2
Grade 2 paraesthesia persisting until next cycle	Reduce oxaliplatin to 65mg/m^2
Grade 3 paraesthesia lasting longer than 7 days	Reduce oxaliplatin to 65mg/m^2
Grade 3 paraesthesia persisting until next cycle	Discontinue oxaliplatin permanently
Grade 4 of any duration	Discontinue oxaliplatin permanently

Specific Information on Administration
Patient needs central line insertion. Assess for PICC prior to commencing treatment
Oxaliplatin should not mix with sodium chloride.

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 erythrodysaesthesia, chest pain or infection.

THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON, CLINICIAN FOR COLO-RECTAL CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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