NHS
North West Coast
Strategic Clinical Networks

Chemotherapy protocol

Drug Regimen
Oxaliplatin and Capecitabine (CAPOX)

Indication for use
Metastatic colorectal cancer

Regimen
Oxaliplatin 130mg/m^2 500ml 5% Glucose IV over 2 hours
Capecitabine 1000mg/m^2 bd x 14 days (maximum 2000 mg bd)

Treatment is repeated every three weeks until disease progression

Investigation prior to initiating treatment
FBC
U&Es
LFT
Bone
CEA
Creatinine clearance
CT scan

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.

Cautions
Avoid cold drinks for 2-3 days after Oxaliplatin infusion.

Investigations and consultations prior to each cycle
FBC, U&Es, LFT, calcium and magnesium before every cycle
Repeat CEA every two cycles

The liver function tests 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 1 or 2 cycles

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.

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 levels defer one week or contact consultant)

Creatinine Clearance >50 ml/min
Neutrophils > 1.5 $x10^9$/l
Platelets > 100 $x10^9$/l
Total bilirubin <3 ULN
ALT, AST < 2.5 ULN
Alk Phos < 2.5 ULN

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

Dose Modification Criteria
Age ≥ 70 years – reduce Capecitabine to 750 mg/m^2 (max 1500 mg bd)

Renal impairment

Creatinine Clearance (ml/min)	Capecitabine	Oxaliplatin dose
>50	100%	100%
30-50	75%	100%
<30	Contraindicated	Omit

Hepatic impairment

Bilirubin >3 xULN or ALT >2.5 ULN : Give 50% capecitabine 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 capecitabine reduction
If delay >1 week reduce capecitabine 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, delay until recovers to grade ≤2 then reduce oxaliplatin dose to 100mg/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 130mg/m^2
Grade 2 paraesthesia persisting until next cycle	Reduce oxaliplatin to 100mg/m^2
Grade 3 paraesthesia lasting longer than 7 days	Reduce oxaliplatin to 100mg/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 must be able to comply with oral chemotherapy regimen

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.
Any unused tablets to be returned at the next appointment

Cycle must finish 14 days after starting irrespective of how many delays or tablets not taken.

Cockroft Formula

Estimated GFR Male $\frac{1.25 \times (140-\text{age}) \times \text{Wt(kg)}}{\text{Serum creatinine (umol/l)}}$

Female $\frac{1.05 \times (140\text{-age}) \times \text{Wt(kg)}}{\text{Serum creatinine (umol/l)}}$

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

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