NHS
North West Coast
Strategic Clinical Networks

Chemotherapy protocol

Drug regimen
Raltitrexed

Indication for use
Metastatic colorectal adenocarcinoma and:
- Unable to tolerate 5-FU (e.g. cardiac problems)
- No prior chemotherapy (unless unexpected early toxicity from 5-FU based regimens)

Regimen

Drug	Route	Fluid	Time
Raltitrexed 3mg/m^2	IV	0.9% sodium chloride 100 ml	15mins

Given every 21 days for 3-6 cycles (NOTE DOSE MODIFICATION CRITERIA IN RENAL IMPAIRMENT)

Investigation prior to initiating treatment
FBC
U&E
LFT
Baseline CEA
Creatinine clearance (use Cockcroft formula)
Performance status 0-2 (PS 3 patients, with stable chronic health problems, may be treated at consultant's discretion)
CT scan

No concurrent, uncontrolled medical illness

Investigations and consultations prior to each cycle
FBC and renal function at each cycle
Patients who develop signs of GI toxicity should have weekly FBC
CEA every 2 cycles

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 cycle

Side Effects
Myelosuppression, diarrhoea, nausea, fatigue, vomiting, stomatitis, poor appetite, plantar palmar erythema, asthenia, fever, rash, sweating, transient elevation of transaminases, infusion reactions, teratogenicity

Acceptable levels for treatment to proceed (if outside these levels defer one week or contact consultant)

Neutrophils >1.5 x 10^9/l
Platelets >100 x 10^9/l
Creatinine Clearance >65ml/min
Bilirubin <10 xULN
ALT/AST <5 x ULN

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

Dose Modification Criteria

Renal impairment

Creatinine clearance	% Dose	Dosing interval
>65 ml/min	full dose	3 weekly
55 – 65 ml/min	75% dose	4 weekly
25 – 54 ml/min	50% dose	4 weekly
<25 ml/min	No therapy	Not applicable

Hepatic impairment

Transient elevations of liver transaminase occur with raltitrexed. No dose modification is needed in mild or moderate impairment, but the liver enzymes should be monitored carefully.

Raltitrexed is not recommended in severe hepatic impairment (bilirubin >10x ULN and or AST/ALT >5x ULN)

Other toxicities

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		

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

Diarrhoea is often associated with immunosuppression so FBC must be checked in grade 3 or 4 diarrhoea.

Any delays should be until the toxicity has resolved to grade 0-1

This is very important and failure to make these adjustments may result in severe, even fatal, toxicity.

This is very important and failure to make these adjustments may result in severe, even fatal, toxicity.

Repeat treatment delays weekly, to a maximum of 3 weeks, until toxicity resolves or blood count recovers fully. If toxicity does not resolve after 3 weeks delay → discontinue treatment

Once a dose reduction has been made, all subsequent doses should be given at the reduced dose.

Specific Information on Administration

- Folinic acid, folic acid or vitamin preparations containing these agents must not be given immediately prior to or during raltitrexed infusion.
- CRO6 and PETACC trials showed an excess of treatment related mortality of raltitrexed compared to 5-FU based regimens. This was, in part, due to patients with poor renal function and **this must be monitored carefully**
- Patients with grade 4 GI (mucositis/diarrhoea) toxicity, or grade 3 GI toxicity with grade 4 haematological toxicity should be managed promptly with IV re-hydration and bone marrow support. Consider folinic acid 25mg/m^2 qds IV until resolution of symptoms.

- Raltitrexed is mutagenic. Pregnancy should be avoided if either partner is receiving raltitrexed. It is also recommended that conception should be avoided for at least 6 months after cessation of treatment

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

Date	**May 2017**
Review	**May 2019**
Version	**11**