Chemotherapy Protocol

**DRUG REGIMEN**
Oxaliplatin and 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)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dose</th>
<th>Volume</th>
<th>Route</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltitrexed</td>
<td>3mg/m²</td>
<td>0.9% Sodium chloride 100ml</td>
<td>IV</td>
<td>15mins</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Followed 45mins later by:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>100mg/m²</td>
<td>5% Glucose 500ml</td>
<td>IV</td>
<td>2 hours</td>
</tr>
</tbody>
</table>

Given every 21 days (BUT NOTE DOSE MODIFICATION CRITERIA) for 3-6 cycles

**Investigation prior to initiating treatment**
U&Es, LFTs, FBC
Baseline CEA, determine measurable/evaluable lesion(s) – clinical/ CXR/ USS or CT scan
Performance status 0-2
Neutrophils >2, platelets >100, bilirubin (1.25 x ULN)
Calculated creatinine clearance and adjust dose according to table below.
No concurrent, uncontrolled medical illness

**Cautions**
See below – NOTE renal failure dose reductions. Avoid cold drinks for 2-3 days after Oxaliplatin infusion.

**Investigations and consultations prior to each cycle**
FBC, Biochemical Profile
Clinic review after each cycle

**Stop treatment if:**
Serum Creatinine >1.5 x upper limit of normal
Neutrophil <2
Platelet <100
Total Bilirubin >3.0 ULN
ALS, AST >2.5 ULN
Alk Phos >2.5 ULN

**Acceptable levels for treatment to proceed** (if outside these levels defer one week or contact consultant)
Retreat at 3 weeks if all (haematological and GI) toxicity has resolved and neutrophils >2 and platelets >100

**Side Effects**
Myelosuppression, diarrhoea, stomatitis, plantar palmar erythema, Peripheral neuropathy
Dose Modification Criteria
Reduce dose based on worst grade toxicity during previous cycle as follows:
Non-haematological toxicity
(e.g. diarrhoea/mucositis)

<table>
<thead>
<tr>
<th>Haem toxicity</th>
<th>Non haem toxicity CTC grade</th>
<th>0-1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2 (P&gt;50, N&gt;1.0)</td>
<td>100%</td>
<td>75%</td>
<td>50%</td>
<td>NFT</td>
<td></td>
</tr>
<tr>
<td>3 (P 10-49, N 0.6-0.9)</td>
<td>75%</td>
<td>75%</td>
<td>50%</td>
<td>NFT</td>
<td></td>
</tr>
<tr>
<td>4 (P&lt;10, N&lt;0.5)</td>
<td>50%</td>
<td>50%</td>
<td>NFT</td>
<td>NFT</td>
<td></td>
</tr>
</tbody>
</table>

(% in table is the % of the full dose to be given)
(P=platelets, N=neutrophils, NFT=no further treatment)

Renal impairment:
For impairment before or during therapy, adjust dose as follows:

<table>
<thead>
<tr>
<th>Creatinine clearance</th>
<th>%Dose</th>
<th>Dosing interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;65 ml/min</td>
<td>Full dose</td>
<td>3 weekly</td>
</tr>
<tr>
<td>55 – 65 ml/min</td>
<td>75% dose</td>
<td>4 weekly</td>
</tr>
<tr>
<td>25 – 54 ml/min</td>
<td>50% dose</td>
<td>4 weekly</td>
</tr>
<tr>
<td>&lt;25 ml/min</td>
<td>No therapy</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

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 give no further 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/m2 qds IV until resolution of symptoms.

THIS PROTOCOL HAS BEEN DIRECTED BY DR SUSNERWALA, CLINICIAN FOR COLORECTAL CANCER

RESPONSIBILITY FOR THIS TEMPLATE LIES WITH THE HEAD OF SERVICE

DATE November 2015
REVIEW November 2017
VERSION 3