5-FLUOROURACIL CONTINUOUS INFUSION

Indication: Adjuvant therapy for resected rectal cancer

Drug/Dosage: 5-Fluorouracil 300mg/m²/24 hours IV Continuous

Administration: Continuous infusion via central venous catheter and ambulatory infusion device.

Frequency: 24 hour continuous infusion for 12 weeks.
Review 3 weekly

Main Toxicities: Mucositis; Diarrhoea; Palmar/Plantar Erythema; Myelosuppression; Coronary artery spasm (see Comments); Ovarian failure/Infertility;

Anti-emetics: Mildly emetogenic

Supportive medication: Loperamide tablets 4mg stat, then 2mg prn for diarrhoea
Pyridoxine tablets 50mg tds, if required for palmar-plantar erythema (PPE)

Extravasation: Non-vesicant

Regular investigations:
- FBC 3 weekly
- LFTs 3 weekly
- U&Es 3 weekly
- CEA 3 weekly

Toxicities and Dose Modifications

Haematological Toxicity

WBC < 2.0 x 10⁹/l
or
Neutrophils < 1.0 x 10⁹/l
or
Platelets < 75 x 10⁹/l
Delay treatment for 1 week

Haematological toxicity is unusual. If it occurs appropriate dose modification should be discussed with consultant.

Renal Impairment
Before every course, calculate CrCl using Cockcroft and Gault. If borderline, an EDTA should be requested.

Creatinine Clearance (ml/min) 5FU Dose
> 50 Give 100% dose
30 – 50 Give 100% dose
< 30 Give 80% dose
Hepatic Impairment

Bilirubin > 3 x ULN
or
ALT/AST > 2.5 ULN

Omit fluorouracil until liver function recovers

Non-Haematological Toxicities

Note that severe diarrhoea and/or severe mucositis early in the first treatment cycle can be the first presenting toxicity due to DPD enzyme deficiency, in which case potentially fatal neutropenia can quickly follow.

Toxicity due to fluorouracil administration may be managed symptomatically and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced, it should not be increased at a later time. Doses of fluorouracil omitted for toxicity are not replaced or restored. Instead the patient should resume the planned treatment cycle.

Diarrhoea, abdo pain,N&V,Stomatitis

<table>
<thead>
<tr>
<th>Grade</th>
<th>Immediate action</th>
<th>Dose next cycle</th>
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</thead>
<tbody>
<tr>
<td>1st appearance</td>
<td>maintain dose</td>
<td>100%</td>
</tr>
<tr>
<td>2nd appearance</td>
<td>100% Interrupt until resolved to grade 0-1</td>
<td>100%</td>
</tr>
<tr>
<td>3rd appearance</td>
<td>75% Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td>4th appearance</td>
<td>50% Discontinue treatment permanently</td>
<td>50%</td>
</tr>
<tr>
<td>1st appearance</td>
<td>75% Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td>2nd appearance</td>
<td>50% Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td>3rd appearance</td>
<td>Discontinue treatment permanently</td>
<td>50%</td>
</tr>
<tr>
<td>1st appearance</td>
<td>Discontinue or at consultants discretion Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
</tbody>
</table>

Palmar-Plantar Erythema

<table>
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</tr>
<tr>
<td>1st appearance</td>
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<td>50%</td>
</tr>
<tr>
<td>2nd appearance</td>
<td>50% Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
</tbody>
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Reason for Update: Network Protocol Development
Version: 2
Supersedes: All other versions
Prepared by: S. Eestila
Approved by Consultant: N. Maisey
Checked by (Network Pharmacist): J. Turner
Approved by SELCN DTAC Chair: Nic Ketley
Date: 06/03/08
Date: 13/07/08
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Cardiotoxicity

Coronary artery spasm is a recognised complication of fluorouracil although the evidence base regarding aetiology, management & prognosis is not particularly strong. The incidence is estimated to be between 2% and 18%. Coronary artery spasm is usually reversible on discontinuing the treatment. Should a patient receiving fluorouracil present with chest pains, stop the treatment. Standard investigation and treatment of angina may be required. If re-challenge is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, fluorouracil should be withdrawn permanently. Refer to Consultant to discuss.

Neurotoxicity

Caution must be exercised in patients with central or peripheral nervous system disease e.g. cerebral metastasis or neuropathy

Drug interactions:
- Coumarin anticoagulants-monitor INR
- Phenytoin- altered plasma levels
- Metronidazole- increased plasma levels and toxicity
- Folinic acid- increased toxicity
- Allopurinol- reduced efficacy
- Antacids- absorption interference

References

Chau, I et al (unpublished), 2004; Gastrointestinal Cancers Symposium; Abstract No: 180
1COIN Guidelines Oct 2000
Royal Surrey County Hospital chemotherapy protocols
www.medicines.org.uk,
Micromedex review, Fluorouracil. Sept2007