Chemotherapy Protocol

COLORECTAL CANCER

FLUOROURACIL and FOLINIC ACID (Modified de Gramont)

Regimen

- Colorectal Cancer– Fluorouracil and Folinic Acid (Modified de Gramont)

Indication

- Treatment of advanced / metastatic colorectal cancer
- Adjuvant treatment of stage II - III colon cancer following surgery
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Fluorouracil	Palmar-plantar erythrodysesthesia, diarrhoea, mucositis, chest pain

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFT's and U&E's prior to day one of treatment
- Patients with complete or partial dihydropyrimidine dehydrogenase (DPD) deficiency are at increased risk of severe and fatal toxicity during treatment with fluorouracil. All patients should be tested for DPD deficiency before initiation (cycle 1) to minimise the risk of these reactions

Dose Modifications

The dose modifications listed are for haematological, liver and renal function only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

Haematological

Prior to prescribing the following criteria must be met;

Criteria	Eligible Level
Neutrophils	Equal to or more than $1.5x10^9$/L
Platelets	Equal to or more than $100x10^9$/L

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL

For haematological toxicity, if the neutrophil count is less than 1.5×10^9/L or the platelet count is less than 75×10^9/L, delay treatment until these levels are achieved. Reinitiate therapy at the full dose for up to a 7 day delay or for a delay of more than 7 days with 75% of the original dose for thrombocytopenia. If neutropenia is the issue, then after 7 days omit the bolus fluorouracil for this and subsequent cycles. If a further delay is necessary despite omitting the bolus fluorouracil then reduce the dose of the infusional fluorouracil to 80% of the original dose. If the delay is 21 days or more then stop therapy.

There is no need to dose adjust the folinic acid for haematological counts.

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes. Dose limiting toxicities include diarrhoea, abdominal pain, emesis, stomatitis and palmar-plantar erythrodysesthesia among others.

Kidney / Liver Impairment

Drug	Hepatic	Renal
Fluorouracil	If the bilirubin is more than 85umol/L and / or the AST more than 180 fluorouracil is contra-indicated. In moderate hepatic impairment consider reducing the dose by 30% and for severe impairment by 50%	A dose adjustment is only required in severe renal impairment

Regimen

14 day cycle for 6 - 12 cycles

Drug	Dose	Days	Route
Fluorouracil	$400mg/m^2$	1	Intravenous bolus over 10 minutes
Fluorouracil	$2800mg/m^2$	1	Intravenous infusion over 46 hours
Folinic Acid	350mg	1	Intravenous infusion in 250ml glucose 5% over 120 minutes

Dose Information

- Fluorouracil will be dose banded in accordance with the national dose bands (25mg/ml PM bolus and 50mg/ml infusion)

Administration Information

Extravasation

- Fluorouracil – inflammitant

Other

- Central venous access and use of an ambulatory infusion pump is required.

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy

  - metoclopramide 10mg oral or intravenous

  As take home medication;

  - metoclopramide 10mg three times a day when required oral

- Oral loperamide 4mg after the first loose stool then 2-4mg four times a day when required for the relief of diarrhoea (maximum 16mg/24 hours).

- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed

Additional Information

- The folinic acid may be replaced with calcium levofolinate 175mg intravenous infusion in 250ml glucose 5% over 120 minutes

References
1. Seymour MT, Wilson G, Dent JT et al. Dose escalation study of a modified “de Gramont” regimen, better suited to the chemotherapy day unit. Ann Oncol (1998);

REGIMEN SUMMARY

Day One

1. Metoclopramide 10mg oral or intravenous

2. Folinic Acid 350mg in 250ml glucose 5% over 120 minutes intravenous infusion

3. Fluorouracil 400mg/m^2 intravenous bolus over 10 minutes

4. Fluorouracil 2800mg/m^2 intravenous infusion over 46 hours

Take Home Medicines

5. Metoclopramide 10mg three times a day when required oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Nov 2020	Updated monitoring with DPD testing Dose banding updated Coding removed	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1.1	May 2014	Header changed Toxicity rating removed Tabulation throughout Renal and hepatic dose reductions updated Bolus removed throughout Fluorouracil bolus administration changed to 10 minutes Pyridoxine removed from supportive therapies Metoclopramide dose changed to 10mg throughout Dexamethasone TTO clarified Disclaimer added	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	Aug 2010	None	Dr Debbie Wright Pharmacist	Dr Tim Iveson Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.