Chemotherapy Protocol

COLORECTAL CANCER

FLUOROURACIL-MITOMYCIN-RADIOTHERAPY

Regimen

- Colorectal Cancer – Fluorouracil-Mitomycin-Radiotherapy

Indication

- Squamous cell carcinoma of the anus
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Fluorouracil	Palmar-plantar erythrodysesthesia, diarrhoea, mucositis, chest pain
Mitomycin	Nephrotoxicity, myelosuppression (cumulative).

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 and twenty-nine 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
Neutrophil	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 10g/dL

Neutrophil and / or Platelets	Dose Modifications	
	Fluorouracil	Mitomycin
NCI-CTC Grade 3	75%	75%
NCI-CTC Grade 4	50%	50%

Hepatic Impairment

Deteriorating liver or kidney function may be a sign of disease progression or drug toxicity.

Drug	Hepatic
Fluorouracil	If the bilirubin is more than 85umol/L and / or the AST more than 180umol/L fluorouracil is contra-indicated. In moderate hepatic impairment consider reducing the dose by 30% and for severe impairment by 50%
Mitomycin	Dose reductions are probably not necessary. It is a clinical decision when the AST level is more than 2xULN

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Fluorouracil	Dose adjustment is only required in severe renal impairment	
Mitomycin	more than 60	$12mg/m^2$
	50 - 59	8mg/m2
	less than 50	contra-indicated

Other

Both fluorouracil and mitomycin should be stopped for any treatment related toxicity sufficient to require interruption of treatment, with completion of the course on recovery.

Fluorouracil

For a NCI-CTC grade 3 diarrhoea reduce the dose to 75%. For a NCI-CTC grade 4 diarrhoea reduce the dose by 50%. Treat symptomatically with oral loperamide at a dose of 2mg every two hours once first liquid stool appears and continue until 12 hours after the last liquid stool. Do not use for longer than 48 hours (maximum daily dose is 16mg).

Regimen

In those aged 71 years and above and / or if there is a significant intercurrent illness the dose of fluorouracil is often reduced to 750mg/m^2/day on days 1,2,3,4 and 29, 30, 31, 32. The mitomycin dose is reduced to 10mg/m^2 (maximum dose 20mg). Always confirm the intended dose with the consultant oncologist responsible for the patients care.

42 day cycle for 1 cycle

Cycle One

Drug	Dose	Days	Route
Fluorouracil	1000mg/m^2/day (total dose is 4000mg/m^2/96hours)	1, 2, 3, 4 and 29, 30, 31, 32	Continuous intravenous infusion over 96 hours using an infusor device in sodium chloride 0.9%
Mitomycin	12mg/m^2 (maximum dose 20mg)	1	Intravenous bolus in water for injection over 10 minutes

Dose Information

- Fluorouracil will be dose banded in accordance with the national dose bands (50mg/ml)
- Mitomycin will be dose rounded to the nearest 1mg (up if halfway)
- The maximum dose of mitomycin is 20mg

Administration Information

Extravasation

- Fluorouracil – inflammitant
- Mitomycin - vesicant

Other

- Central venous access and use of an ambulatory infusion pump is required
- The fluorouracil infusion should be started at least two hours before administration of the radiotherapy

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy on **day one** only

  - dexamethasone 8mg oral or intravenous
  - metoclopramide 10mg oral or intravenous

  As take home medication

  - dexamethsone 4mg once a day for three days
  - metoclopramide 10mg three times a day when required oral

- Oral loperamide 2mg every two hours once first liquid stool appears and continue until 12 hours after the last liquid stool. Do not use for longer than 48 hours (maximum daily dose is 16mg).

- Ciprofloxacin 250mg twice a day for 42 days oral

- 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

References
1. Melcher AA, Sebag-Montefiore D et al. Concurrent chemoradiotherapy for squamous cell carcinoma of the anus using a shrinking field radiotherapy technique without a boost. BMJ 2003; 88 (9): 1352-1357.

REGIMEN SUMMARY

Fluorouracil-Mitomycin RT

The fluorouracil infusion must be started at least two hours before administration of the radiotherapy.

Day One

1. Dexamethasone 8mg oral or intravenous

2. Metoclopramide 10mg oral or intravenous

3. Mitomycin 12mg/m^2 intravenous bolus in water for injections over 10 minutes (maximum dose 20mg)

4. Fluorouracil 4000mg/m^2 continuous intravenous infusion over 96 hours in sodium chloride 0.9%

Take Home Medicines

5. Ciprofloxacin 250mg twice a day oral for 42 days

6. Dexamethasone 4mg once a day oral for 3 days

7. Metoclopramide 10mg three times a day when required oral
   Administration Instructions
   Please supply two original packs or 60 tablets for days 1 and 29

Day Twenty-Nine

1. Metoclopramide 10mg oral or intravenous bolus

2. Fluorouracil 4000mg/m^2 continuous intravenous infusion over 96 hours in sodium chloride 0.9%

Take Home Medicines

3. Metoclopramide 10mg three times a day when required oral
   Administration Instructions
   This will be supplied on day one and will not appear on Aria as part of the regimen

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Nov 2020	Updated monitoring with DPD testing Dose banding updated Coding removed Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Aug 2014	None	Dr Debbie Wright Pharmacist	Dr V McFarlane Consultant Clinical 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.