Chemotherapy Protocol

BLADDER CANCER

FLUOROURACIL-MITOMYCIN-RADIOTHERAPY

Regimen

- Bladder Cancer – Fluorouracil-Mitomycin-Radiotherapy

Indication

- Muscle invasive bladder cancer
- 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, LFTs and U&Es prior to day one and sixteen 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.

The dose of chemotherapy should be adjusted or the agents omitted before any adjustments in radiotherapy are made in relation to adverse effects.

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

Hepatic / Renal Impairment

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

Drug	Hepatic	Renal
Fluorouracil	If the bilirubin is more than 85µmol/L and / or the AST more than 180µmol/L 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
Mitomycin	Dose reductions are probably not necessary. It is a clinical decision when the AST level is more than 2xULN	If the creatinine clearance is less than 10ml/min administer 75% of the original dose

Other

Chemotherapy should be stopped for any NCI-CTC grade 4 toxicity. The fluorouracil infusion should be discontinued if there is any NCI-CTC grade 3 toxicity.

Fluorouracil

Grade 1	***Grade 2***	***Grade 3***	***Grade 4***
Diarrhoea			
No Change	Reduce infusion dose by 125mg/m^2/day. Continue radiotherapy.	Discontinue infusion permanently. Consider interrupting radiotherapy (until symptoms resolve to NCI-CTC grade 1)	Stop all therapy. Re-assess weekly.
Mucositis			
No Change	Reduce infusion dose by 125 mg/m^2/day. Continue radiotherapy.	Discontinue infusion permanently. Continue radiotherapy unless diarrhoea also present.	Stop all therapy. Reassess weekly.

Regimen

1 cycle of 26 days (radiotherapy is given as 64 Gy in 32 fractions over 45 days)

Drug	Dose	Days	Route
Fluorouracil	500mg/m^2/day (total dose is 2500mg/m^2/120hours)	1, 2, 3, 4, 5 and 22, 23, 24, 25, 26	Continuous intravenous infusion over 120 hours using an infusor device in sodium chloride 0.9% starting on day 1 and 22
Mitomycin	12mg/m^2	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)

Administration Information

Extravasation

- Fluorouracil - inflammitant
- Mitomycin - vesicant

Other

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

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

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

  15-30 minutes prior to chemotherapy on **day twenty-two** only

  - metoclopramide 10mg oral or intravenous

- 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).

- 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. James ND, Hussein AS, Hall E et al. Radiotherapy with or without chemotherapy in muscle invasive bladder cancer. N Engl J Med 2012; 366: 1477-1488.

REGIMEN SUMMARY

Fluorouracil-Mitomycin RT

Day 1

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

4 Fluorouracil 500mg/m^2/day continuous intravenous infusion over 120 hours in sodium chloride 0.9%

Take Home Medicines

5 Dexamethasone 4mg once a day oral for 3 days starting the day after mitomycin

6 Metoclopramide 10mg three times a day when required oral
Administration Instructions
Please supply 10 days or an original pack if appropriate to cover day 1 and 22

Day 22

7 Metoclopramide 10mg oral or intravenous

8 Fluorouracil 500mg/m^2/day continuous intravenous infusion over 120 hours in sodium chloride 0.9%

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 2015	Treatment updated to days 1-5 and 22-26 in all sections of the protocol. Metoclopramide admin instructions updated	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Feb 2014	None	Dr Deborah Wright Pharmacist	Dr P Fenton 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 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.