**Chemotherapy Protocol**

## ANAL CANCER

## CAPECITABINE-MITOMYCIN-RADIOTHERAPY

### Regimen

- Anal Cancer – Capecitabine-Mitomycin-Radiotherapy

### Indication

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

### Toxicity

| Drug | Adverse Effect |
|---|---|
| Capecitabine | 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 then every seven days during treatment
- Patients with complete or partial dihydropyrimidine dehydrogenase (DPD) deficiency are at increased risk of severe and fatal toxicity during treatment with capecitabine. 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 or the prescription of an erythropoietin produce according to NICE TA 323 if the patient is symptomatic of anaemia or has a haemoglobin of less than 10g/dL.

| Neutrophil and / or Platelets | Dose Modifications | |
|---|---|---|
| | Capecitabine | 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 |
|---|---|
| Capecitabine | There is a lack of information available. In patients with mild to moderate hepatic dysfunction due to liver metastases, 100% of the dose is probably acceptable. |
| | |
| 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) |
|---|---|---|
| Capecitabine | 51-80 | 100 |
| | 30-50 | 75 |
| | less than 30 | contra-indicated |
| | | |
| Mitomycin | more than 60 | $12mg/m^2$ |
| | 50 - 59 | 8mg/m2 |
| | less than 50 | contra-indicated |

### *Other*

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

*Capecitabine*

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. If chest pain occurs consider stopping capecitabine.

NCI-CTC Grade 2

Interrupt treatment until the toxicity resolves to NCI-CTC grade 0-1 then continue at the same dose. If the toxicity recurs for a second time again interrupt treatment until it resolves to NCI-CTC grade 0-1 then resume therapy at 75% of the original dose. If the same adverse effect develops on a third occasion once more interrupt treatment until it resolves to NCI-CTC grade 0-1 then continue at 50% of the original dose. Stop treatment if the toxicity re-appears on a fourth instance.

NCI-CTC Grade 3

Interrupt treatment until the toxicity resolves to NCI-CTC grade 0-1 then continue treatment using 75% of the original dose with prophylaxis if appropriate. If the toxicity recurs for a second time again interrupt treatment until it resolves to grade 0-1 and then resume therapy at 50% of the original dose. If the same adverse effect develops on a third occasion discontinue capecitabine.

NCI-CTC Grade 4

Discontinue treatment unless the responsible consultant considers it to be in the best interest of the patient to continue at 50% of the original dose once the toxicity has resolved to grade 0-1.

When capecitabine is stopped for toxicity the doses are omitted, not delayed.

Regimen

In those aged 71 years and above and / or if there is a significant intercurrent illness the dose of capecitabine may be reduced to 500mg/m$^2$. 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**

| Drug | Dose | Days | Route |
|---|---|---|---|
| Capecitabine | 825mg/m$^2$ twice a day | 1-5, 8-12, 15-19, 22-26, 29-33, 36-38 (28 days in total, to be given on the days of radiotherapy only) | Oral |
| Mitomycin | 12mg/m$^2$ (maximum dose 20mg) | 1 | Intravenous bolus in water for injection over 10 minutes |

## Dose Information

- Capecitabine should be given on the days of radiotherapy only
- Capecitabine will be dose banded in accordance with the national dose bands
- Mitomycin  will be dose rounded to the nearest 1mg (up if halfway)
- The maximum single dose of mitomycin is 20mg
- The maximum cumulative dose of mitomycin is 28mg/$m^2$ or 56mg

## Administration Information

### *Extravasation*

- Mitomycin - vesicant

### *Other*

## 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
- Mouthwashes according to local or national policy on the treatment of mucositis.
- Gastric protection with a proton pump inhibitor or $H_2$ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

## Additional Information

- The National Patient Safety Agency alert NPSA/2008/RRR001 must be followed when prescribing, dispensing or administering oral chemotherapy.

- Ensure the total daily dose of capecitabine is divided into two doses given twelve hours apart (the first should be administered in the evening of day one of the cycle) Serious toxicity has occurred where the total daily dose has been given twice a day.

- It must be made clear to all staff, including those in the community, that this is a short course of oral chemotherapy that must not be continued.

References

1. Glynne-Jones R, Meadows H, Wan S et al. EXTRA – a multicentre phase II study of chemoradiation using a five day per week oral regimen of capecitabine and IV mitomycin in anal cancer. Int J Radiat Oncol Biol Phy 2008; 72 (1): 119-126.

**REGIMEN SUMMARY**

**Capecitabine-Mitomycin RT**

## 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)

## Take Home Medicines

4. Capecitabine 825mg/$m^2$ twice a day on the days of radiotherapy (days 1-5, 8-12, 15-19, 22-26, 29-33, 36-38 – 28 days in total)
Administration Instructions
To be taken on the days of radiotherapy only. (The total numbers of days of capecitabine treatment is 28).

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

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

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

## DOCUMENT CONTROL

| Version | Date | Amendment | Written By | Approved By |
|---|---|---|---|---|
| 1.1 | Nov 2020 | Updated monitoring with DPD testing<br>Dose banding statement updated<br>Coding removed | Donna Kimber<br>Pharmacy Technician | Rebecca Wills<br>Pharmacist |
| 1 | May 2015 | None | Dr Debbie Wright<br>Pharmacist | Dr V McFarlane<br>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.