

**Systemic Anti Cancer Treatment Protocol**

**Mitomycin C and Fluorouracil  
With XRT chemo radiation Anal  
(MMC+5FU anal XRT)**

**PROTOCOL REF: MPHAMCFXGA  
(Version No: 1.0)**

**Approved for use in:**

Localised squamous carcinoma of the anus

**Dosage:**

A single cycle only with concurrent radiotherapy

| Drug         | Dosage                                     | Route    | Frequency                |
|--------------|--|----------|--------------------------|
| Mitomycin C  | 12mg/m <sup>2</sup>                        | IV bolus | Day 1                    |
| Fluorouracil | 1000mg/m <sup>2</sup> /24 hours for 4 days | IV       | Days 1 to 4 and 25 to 29 |

For patients with a poorer performance status consider reducing the dose of fluorouracil to 750mg/m<sup>2</sup>/24hour and Mitomycin C to 10mg/m<sup>2</sup>

**Supportive treatments:**

Anti emetic risk – low

Domperidone 10mg oral tablets, up to 3 times a day or as required

Loperamide 4mg initially then 2mg after each loose stool

**Extravasation risk:**

Mitomycin-C – vesicant – follow Network extravasation policy. Specific treatment available

Fluorouracil is IRRITANT and should be treated using Network guidance

|  |                                |                                |
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## Administration:

| Day      | Drug         | Dosage                         | Route | Diluent and Rate   |
|----------|--------------|--------------------------------|-------|--|
| 1        | Mitomycin C  | 12mg/m <sup>2</sup>            | IV    | Bolus via fast running infusion of 0.9% Sodium chloride    |
| 1 to 4   | Fluorouracil | 1000mg/m <sup>2</sup> /24hours | IV    | LV 2 yellow ambulatory infusion device (2ml/hr) over 4days |
| 25 to 29 | Fluorouracil | 1000mg/m <sup>2</sup> /24hours | iv    | LV 2 yellow ambulatory infusion device (2ml/hr) over 4days |

## Interactions

Care with patients on coumarin anticoagulants – monitor INR closely, consider LMWH  
Sorivudine and analogues – Potentially fatal interaction – avoid completely

**Medical/Nursing review** as per patient management plan

**For severe reactions, discuss with Consultant before continuing with treatment.**

## Main Toxicities:

Mitomycin-C – myelosuppression, haemolytic uremic syndrome, pulmonary toxicity, diarrhoea, constipation, stomatitis, cholecystitis, jaundice, acute renal failure and proteinuria

Haemolytic Uraemic Syndrome consists of microangiopathic haemolytic anaemia, renal failure thrombocytopenia, and hypertension. Patients are at greater risk if they have renal failure, evidence of red cell fragmentation and if they have received several courses of treatment with cumulative doses of Mitomycin-C >36mg/m<sup>2</sup>. Where suspected, test for red cell fragmentation. HUS may be treated with Prednisolone 30mg once daily for one week to prevent worsening haemolysis.

Patient should be discussed with renal team.

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Fluorouracil- Diarrhoea, Nausea and vomiting, conjunctivitis / sore eyes, skin rashes, Palmar Plantar Erythema (PPE or hand foot syndrome), stomatitis, chest pain (myocardial ischaemia or angina), ovarian failure / infertility, nail ridges, taste changes

DPD deficiency – leads to severe early fluorouracil toxicity, affects approximately 3% of population, may be life threatening

## Investigations and treatment plan

|   | Pre | Day 1 | Day 25 |
|---|-----|-------|--------|
| Medical / Senior Nurse / AHP Assessment | X   |       | X      |
| Nursing Assessment                      |     | X     | X      |
| FBC                                     | X   | X     | X      |
| U&E & LFT                               | X   | X     | X      |
| CT scan                                 | X   |       |        |
| Informed Consent                        | X   |       |        |
| ECG                                     | X   |       |        |
| Blood pressure measurement              | X   | X     | X      |
| PS recorded                             | X   | X     | X      |
| Toxicities documented                   | X   | X     | X      |
| Weight recorded                         | X   | X     | X      |

## Dose Modifications and Toxicity Management:

### Haematological toxicity

Proceed on day 1 and day 25 if:-

|                              |                                    |
|------------------------------|------------------------------------|
| ANC $\geq 1.0 \times 10^9/L$ | Platelets $\geq 100 \times 10^9/L$ |
|------------------------------|------------------------------------|

|  |                                |                                |
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Discuss with consultant oncologist if blood results are below these recommended limits

**Non-haematological toxicity**

| Recommended dose reduction | Fluorouracil   |
|----------------------------|--|
| Grade 2                    | Reduce all subsequent doses of fluorouracil by 20%               |
| Grade 3                    | Discontinue chemotherapy; consider interruption in radiotherapy. |
| Grade 4                    | Discontinue treatment  |

**Hepatic impairment:**

| Mitomycin-C   |                   |                      |
|---|-------------------|----------------------|
| Clinical decision when AST levels > 2 x ULN. Clearance is primarily by metabolism in the liver, with approximately 10% of a dose excreted unchanged in the urine. |                   |                      |
| Fluorouracil  |                   |                      |
| Bilirubin<br>/µmol/L  | AST/ALT<br>/units | Dose                 |
| <85   | and <180          | No dose modification |
| >86   | or >181           | Contra indicated     |

**Renal impairment:**

| CrCl (mL/min) | Fluorouracil       |
|---------------|--------------------|
| Above 30      | 100% dose          |
| Below 30      | Consider reduction |

| CrCl (mL/min) | Mitomycin-C |
|---------------|-------------|
| > 60          | 100% dose   |
| 10 to 60      | 80% dose    |
| <10           | 60% dose    |

**Non-haematological toxicity**

No second dose of mitomycin given in this regimen

| Fluorouracil                |  |
|-----------------------------|--|
| Chest pain, coronary artery | Stop fluorouracil, standard angina investigations, refer to consultant, if symptoms persist stop permanently |

| spasm                         |   |   |   |   |         |         |                               |   |   |   |   |
|-------------------------------|---|---|---|---|---------|---------|-------------------------------|---|---|---|---|
| Stomatitis                    | If mouth ulcers or > grade 2 symptoms develop treat symptomatically as per UKONS guide<br>Delay treatment until resolved to grade 1 and reduce fluorouracil doses by 20%.   |   |   |   |         |         |                               |   |   |   |   |
| Diarrhoea                     | Monitor increase of bowel/stoma output over pre-treatment normal.<br>Treat diarrhoea between cycles symptomatically as per UKONS guide.<br>Treat diarrhoea between infusions symptomatically. If diarrhoea remains troublesome reduce dose by 20%<br><table border="1" data-bbox="467 562 1401 1003"> <thead> <tr> <th>Grade 0</th> <th>Grade 1</th> <th>Grade 2</th> <th>Grade 3</th> <th>Grade 4</th> </tr> </thead> <tbody> <tr> <td>None or no change from normal</td> <td>Increase of up to 3 bowel movements a day over pre-treatment normal or mild increase in ostomy output</td> <td>Increase of up to 4-6 episodes a day or moderate increase in ostomy output or nocturnal movement or moderate cramping</td> <td>Increase of up to 7-9 episodes a day or severe increase in ostomy output or incontinence / severe cramping / bloody diarrhoea</td> <td>Increase &gt;10 episodes a day or grossly bloody diarrhoea</td> </tr> </tbody> </table> | Grade 0   | Grade 1   | Grade 2   | Grade 3 | Grade 4 | None or no change from normal | Increase of up to 3 bowel movements a day over pre-treatment normal or mild increase in ostomy output | Increase of up to 4-6 episodes a day or moderate increase in ostomy output or nocturnal movement or moderate cramping | Increase of up to 7-9 episodes a day or severe increase in ostomy output or incontinence / severe cramping / bloody diarrhoea | Increase >10 episodes a day or grossly bloody diarrhoea |
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| PPE                           | Reduce fluorouracil by 20% for subsequent doses if persistent troublesome PPE. See table  |   |   |   |         |         |                               |   |   |   |   |

## References:

James, RD et al; Mitomycin or cisplatin chemoradiation with or without maintenance chemotherapy for treatment of squamous-cell carcinoma of the anus (ACT II): a randomised, phase3, open label, 2 x 2 factorial trial. Lancet Oncology 2013; 14(6):5 16-24

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