

Chemotherapy protocol

Drug regimen

Mitomycin-C & capecitabine

Indication for use

Palliative chemotherapy for colorectal cancer

Regimen

Mitomycin-C (MMC) – 7mg/m² on day 1 (max 14 mg)

Capecitabine 625mg/m² bd for 6 weeks

(Maximum 4 cycles – total MMC dose 28mg/m², max 56mg)

Cycle to be repeated every six weeks

Investigation prior to initiating treatment

FBC

U&E

LFT

CEA

Creatinine clearance

CT scan

Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism (this can present as severe diarrhoea and/or severe stomatitis early in the first cycle). Patients require DPD testing prior to administration. Dose adjustments should be made in accordance with local DPD policy.

Investigations and consultations prior to each cycle

FBC, U&E, LFT, CEA, creatinine clearance every six weeks

The liver function tests may be retrospectively looked at (i.e. after the chemotherapy treatment) **unless** they are known to be abnormal then they need to be repeated the day before so that the results are available pre-chemotherapy.

Acceptable levels for treatment to proceed

(if outside these levels defer one week or contact consultant)

Acceptable blood range: neutrophils $\geq 1.5 \times 10^9/l$, platelets $\geq 100 \times 10^9/l$,

If only Hb is low (below 95g/dl) please contact doctor to arrange for blood transfusion but continue with chemotherapy

If neutrophils $1.2 - 1.5 \times 10^9/l$ contact consultant

Creatinine clearance ≥ 60 ml/min

If U&Es abnormal contact consultant

Side Effects

Tiredness, diarrhoea and abdominal pain, nausea and vomiting, sore mouth/stomatitis, poor appetite, myelosuppression and thrombocytopenia, skin reaction, hand foot syndrome, conjunctivitis, cardiotoxicity (including coronary artery spasm, angina and tachycardia), ocular toxicity (excessive lacrimation, visual change, photophobia), interstitial lung disease, infusion reactions, veno-occlusive disease, hair loss, haemolytic uraemic syndrome, ovarian failure/infertility, transient cerebellar syndrome, confusion

Dose Modification Criteria

Renal impairment

CrClearance (mL/min)	Mitomycin C (day 1 only)
≥ 60	100% dose

30-59	75% dose
<30	50% dose or omit

CrClearance (ml/min)	Capecitabine
>50	100% dose
30-50	75% dose
<30	Omit

Hepatic impairment

Dose modification may be required. Capecitabine has not been studied in severe hepatic dysfunction

Other toxicities

Haemolytic Uraemic Syndrome (HUS)	Microangiopathic haemolytic anaemia, renal failure, thrombocytopenia and hypertension. More common with cumulative doses of mitomycin C >36mg/m ² If suspected test for red cell fragmentation Discuss with renal team Consider prednisolone 30mg OD for 7 days to prevent worsening haemolysis	
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Toxicity grade	1 st dose event	2 nd dose event	3 rd dose event	4 th dose event
0-1	100%	100%	100%	100%
2	Delay* then 100%	Delay * then 75%	Delay * then 50%	discontinue
3	Delay* then 75%	Delay * then 50%	discontinue	discontinue
4	Discontinue or delay * then 50%	discontinue	discontinue	discontinue

* Stop treatment immediately and delay until toxicity resolved to grade 0-1

Monitor patients with diarrhoea until symptoms completely resolved as rapid deterioration may occur.

Specific Information on Administration

Mitomycin C is given as a bolus injection and is vesicant, avoid extravasation

Patient must be able to comply with oral chemotherapy regimen

Patients should be informed of the need to interrupt treatment immediately if they develop moderate or severe side effects, particularly diarrhoea (not controlled by loperamide), palmar plantar erythrodysesthesia, chest pain or infection.

Any unused tablets to be returned at the next appointment

Cockcroft Formula

Estimated GFR Male $\frac{1.25 \times (140 - \text{age}) \times \text{Wt(kg)}}{\text{Serum creatinine (umol/l)}}$

Female $\frac{1.05 \times (140 - \text{age}) \times \text{Wt(kg)}}{\text{Serum creatinine (umol/l)}}$

**THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON, CLINICIAN FOR COLORECTAL CANCER
RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE**

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