

Mitomycin C and capecitabine with concurrent radiotherapy

Indication

Anal cancer
Vulval cancer

Regimen details

Mitomycin 12mg/m² IV bolus

Capecitabine 825mg/m² bd commencing on day 1 of radiotherapy and continues for 5½ weeks (duration of radiotherapy) taken on radiotherapy days ONLY (usually Monday to Friday)

Cycle frequency

Single cycle

Number of cycles

Single cycle

Administration

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

Patient must be able to comply with oral chemotherapy regimen

Hb must be maintained at 120g/l. If Hb low proceed with chemotherapy but arrange for transfusion within 2 working days

Pre-medication

Not normally required

Emetogenicity

Minimal

Additional supportive medication

Loperamide

Extravasation

Mitomycin is a vesicant

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Bone profile	14 days

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 –pre subsequent cycles

FBC weekly

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	$\geq 1.5 \times 10^9/L$ (contact consultant if 1.2-1.5)
Platelet count	$\geq 100 \times 10^9/L$ (contact consultant if <100)
Haemoglobin (Hb)	≥ 120 g/L (if ≤ 120 g/L proceed with treatment but arrange blood transfusion)
Creatinine clearance	≥ 60 mL/min (see dose modifications below)
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN

Dose modifications

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 $>36\text{mg/m}^2$ 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.

Adverse effects –

for full details consult product literature/ reference texts

Sore mouth, nausea/sickness, pain in abdomen, diarrhoea, skin reaction, conjunctivitis, myelosuppression, neutropenia, thrombocytopenia, cardiac toxicity, ocular toxicity, interstitial lung disease, HUS, diarrhoea and constipation, fatigue, mild alopecia

Significant drug interactions

– for full details consult product literature/ reference texts

Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin. Avoid combination. Switch to low molecular weight heparin if possible.

Avoid concomitant use of capecitabine and allopurinol

Additional comments

Cardiotoxicity has been associated with fluoropyrimidine therapy, with adverse events being more common in patients with a prior history of coronary artery disease. Caution must be taken in patients with a history of significant cardiac disease, arrhythmias or angina pectoris

References

Xeloda SPC - <https://www.medicines.org.uk/emc/product/9081/smpc>

Mitomycin SPC - <https://www.medicines.org.uk/emc/product/1955>

THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON, DESIGNATED LEAD CLINICIAN FOR ANAL CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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