NHS
North West Coast
Strategic Clinical Networks

Chemotherapy protocol

Drug regimen
MCX (Mitomycin C, Cisplatin, Capecitabine)

Indication for use
Metastatic/inoperable Anal Cancer

Regimen
MCX (Mitomycin, Cisplatin, Capecitabine)

Day	Drug	Route	Fluid	Time
Day 1 (alternate cycles ie 6 weekly)	Mitomycin C 7mg/m^2	IV Bolus		
Day 1	KCl 20mmol & $MgSO_4$ 10mmol	IV	1 litre 0.9% NaCl	2 hours
Day 1	Cisplatin 60mg/m^2	IV	500ml 0.9% NaCl	1 hour
Day 1	KCl 20mmol & $MgSO_4$ 10mmol	IV	1 litre 0.9% NaCl	2 hours
Day 1-21	Capecitabine 625mg/m^2 bd	Orally		

Every 3 weeks until disease progression.
Mitomycin C must only be given for a maximum of 3 doses

Investigation prior to initiating treatment
FBC
Biochemistry profile and magnesium
Audiometry (at discretion of consultant)
Calculated creatinine clearance (CrCl)

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
Biochemical profile and magnesium
Calculated Creatinine clearance

Acceptable levels for treatment to proceed (if outside these levels defer one week or contact consultant)

Platelets $\geq$ 100 x10^9/l and neutrophils $\geq$ 1.5 x10^9/l
$Cl_{Cr} \geq$ 60mls/min

If neutrophils 1.2-1.5 x10^9/l contact **consultant**

Side Effects
Sore mouth, nausea/sickness, pain in abdomen, diarrhoea, skin reaction, conjunctivitis, myelosuppression, neutropenia, thrombocytopenia, renal failure, high tone and hearing loss, cardiac toxicity, ocular toxicity, interstitial lung disease, HUS, diarrhoea and constipation, fatigue, mild alopecia.

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)	Cisplatin
≥60	100%
45-59	75%
<45	Omit (consider carboplatin AUC5)

CrClearance (mL/min)	Capecitabine
≥50	100% dose
30-49	75% dose
<30	Omit

Hepatic impairment

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

If transaminases >5x ULN withhold cisplatin until < grade 2 (no liver metastases) or grade 2 or less for patients with liver metastases and baseline elevated transaminases

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 call fragmentation Discuss with renal team Consider prednisolone 30mg OD for 7 days to prevent worsening haemolysis

Toxicity grade	1st dose event	2nd dose event	3rd dose event	4th 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.

Discontinue cisplatin if new functional deterioration in hearing or high frequency hearing loss on audiogram
Discontinue cisplatin if grade 3 sensory or motor neuropathy, and interrupt treatment if grade 2 until resolves to grade 1 (then reduce cisplatin to 50mg/m^2)

Consider 25% dose reduction of mitomycin and cisplatin if symptomatic neutropenia or repeated deferrals

Consider MCF treatment (i.e. substituting 5FU for capecitabine) in patients with severe diarrhoea.

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

Continue Cisplatin/Capecitabine if needed, once the maximum 3 doses of mitomycin has been received.

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

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