North West Coast
Strategic Clinical Networks

Chemotherapy protocol

Drug regimen
Mitomycin C and 5-Fluorouracil with concurrent radiotherapy

Indications for use
Anal carcinoma

Regimen
Day 1 only
Mitomycin C 12mg/m^2 bolus
(max dose 20mg)

Day 1 to 4 and 29 to 32
5-Fluorouracil 1000mg/m^2/day in a continuous infusor for 4 days

WITH CONCURRENT RADIOTHERAPY

Investigation prior to initiating treatment
FBC, LFT, U&Es, Bone, Creatinine clearance

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 weekly
U&Es and LFTs weekly
Consultation every week in radiotherapy department

Acceptable limits for treatment to proceed
(if outside these delay one week or contact consultant)
Acceptable blood range: haemoglobin ≥120g/l, neutrophils ≥1.5 x10^9/l, platelets ≥100 x10^9/l,
If Hb <120 g/l proceed but arrange blood transfusion
If neutrophils 1.2 – 1.5 x10^9/l, contact consultant
If platelets <100 x10^9/l, contact consultant
If U&Es abnormal contact consultant

Side Effects
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.

Dose Modification Criteria

Renal impairment

CrClearance (mL/min)	Mitomycin C (day 1 only)	Fluorouracil
≥60	100% dose	100% dose
10-59	75% dose	100% dose
<10	50% dose or omit	Consider dose reduction

Hepatic impairment

Bilirubin (x ULN)		ALT (xULN)	Mitomycin C Day 1 only	Fluorouracil
≤1.5	and	**≤1.5**	100% dose	100% dose
1.5 – 2.9	or	1.5-2.9	100% dose	67% dose*
3- 5	or	3-5	100% dose	50% dose*
>5	or	>5		contraindicated

*fluorouracil doses may be increased to 100% if no further toxicity

Other toxicities

Toxicity	Definition	Dose adjustment
Stomatitis/Mucositis	Grade 2	Reduce all subsequent fluorouracil to 75% dose
	Grade 3	Reduce all subsequent fluorouracil to 50% dose
	Grade 4	Discontinue all treatment
Diarrhoea*	Grade 2	Reduce all subsequent fluorouracil to 75% dose
	Grade 3	Reduce all subsequent fluorouracil to 50% dose
	Grade 4	Discontinue all treatment
Palmar Plantar Erythrodysthesia	Grade 2	Reduce all subsequent fluorouracil to 75% dose
	Grade 3/4	Reduce all subsequent fluorouracil to 50% dose
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	

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

Specific Information on Administration

- PICC line required
- Mitomycin C is given as a bolus injection and is vesicant, avoid extravasation
- 5-Fluorouracil should be administered as a 24 hour infusion
- The infusion should commence 2 hours prior to the first fraction of radiotherapy
- Hb must be maintained at 120 g/l. If Hb low proceed with chemotherapy but arrange for transfusion within 2 working days

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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