NHS
North West Coast
Strategic Clinical Networks

Chemotherapy protocol

Drug regimen
Mitomycin-C and 5-fluorouracil

Indication for use
Palliative chemotherapy for colorectal cancer

Regimen
Mitomycin-C (MMC) – 7mg/m^2 on day 1 (max 14 mg)
5FU – 300mg/m^2/day x 6 weeks with continuous infusion (change infusor every week)

(Maximum 4 cycles – total Mitomycin C dose 28mg/m^2, 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&Es, LFT every six weeks

Acceptable levels for treatment to proceed
(if outside these delay one week or contact consultant)
Acceptable blood range: neutrophils ≥1.5 x10^9/l, platelets ≥100 x10^9/l,
If Hb <90 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
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, thrombophlebitis

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

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

Specific Information on Administration

Mitomycin C is given as a bolus injection and is vesicant, avoid extravasation
PICC line is required for continuous 5FU administration

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 erythrodyaesthesia, chest pain or infection.

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

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