MITOMYCIN C, CAPECITABINE + RADIOTHERAPY

Chemo-radiotherapy for squamous cell carcinoma of the anus

Drug/Dosage:	Mitomycin C	12mg/m^2	IV	Day 1 **only**
	Capecitabine	825mg/m^2	PO	twice daily on Mondays - Fridays for 5½ - 6 weeks, during RT
	Patients aged > 70 years, or those with significant inter-current illness:			
	Mitomycin C	10mg/m^2	IV	Day 1 **only**
	Capecitabine	825 mg/m^2	PO	twice daily on Mondays - Fridays for 5½ - 6 weeks, during RT

Radiotherapy: 50.4Gy given as 28 fractions (1.8Gy/fraction) on Mondays to Fridays for 5½ weeks

Administration: Mitomycin C via fast running infusion of 0.9% sodium chloride.
Capecitabine is available as 500mg and 150mg tablets, and should be swallowed with water within 30 minutes after a meal.
The first dose of capecitabine should be taken **at least** 1 - 2 hours before the first fraction of radiotherapy.
The last capecitabine dose should be taken on the evening of the last day of radiotherapy.

Note: Patients should be counselled to only take capecitabine on the days when radiotherapy is being given, and not on any other day.
i.e. number of days of capecitabine is equal to number of fractions of RT.

Frequency: One course of chemo-radiotherapy over 5½ - 6 weeks
Clinical review weekly

Main toxicities: myelosuppression; mucositis; diarrhoea; palmar/plantar erythema radiation fibrosis / necrosis of perineum; haemolytic uraemic syndrome; coronary artery spasm (see Comments); ovarian failure/infertility; impotence (males); urinary frequency/cystitis

Anti-emetics: mildly emetogenic

Extravasation: mitomycin C is a vesicant

Regular Investigations:	FBC	weekly (N.B. see Dose Modifications for Hb monitoring)
	U&Es & LFTs	Day 1 and during Week 3 & Week 5
	LFTs	Day 1 and during Week 3 & Week 5
	ECG	If previous history of angina, MI or rhythm disturbances

Comments: Maximum cumulative dose of mitomycin C = 28mg/m^2 or 56mg total dose.

Haemolytic uraemic syndrome is a complication of mitomycin C. Therefore, monitor renal function carefully and request Red Cell Fragments on peripheral blood films if in doubt.

Reason for Update: wording for patient counselling updated	Approved by Consultant: Dr S Cummins
Version: 3	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 2	Date: 22.1.14
Prepared by: S Taylor	Checked by: C Tucker

Dose Modifications

Haematological Toxicity:	Neutrophils < 1.0 x 10^9/l or Platelets < 75 x 10^9/l	Omit capecitabine for 1 week. **Inform Consultant - chemotherapy must not be omitted without Consultant approval.**

Haemoglobin (Hb) needs to be maintained above 12g/dl throughout this treatment. If the Hb falls below this level, a blood transfusion needs to be arranged (treatment may continue).

Non-Haematological Toxicities:

Note that severe diarrhoea and/or severe mucositis early in the first treatment cycle can be the first presenting toxicity due to DPD enzyme deficiency, in which case potentially fatal neutropenia can quickly follow.

Toxicity due to capecitabine may be managed symptomatically and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced, it should not be increased at a later time. Doses of capecitabine omitted for toxicity are not replaced or restored. Instead the patient should resume the planned treatment cycle.

If first appearance of Grade 3/4, or second appearance of Grade 2 toxicity, such as mucositis, PPE or diarrhoea, capecitabine treatment should be interrupted until the toxicity has resolved to ≤ Grade 1. A dose reduction for capecitabine should then be considered. If in doubt, discuss with Consultant.

Radiotherapy-related Toxicities: If radiotherapy is interrupted for any reason, the patient should also stop their capecitabine throughout the RT interruption.

Renal Impairment: Calculate creatinine clearance using Cockcroft and Gault. If borderline, an EDTA should be requested.

Creatinine Clearance (ml/min)	Capecitabine Dose
≥ 30	Give 100% dose
< 30	Omit

CrCl (ml/min)	Mitomycin C Dose
> 10	Give 100%
< 10	Give 75%

Hepatic Impairment:	Bilirubin > 3 x ULN or ALT/AST > 2.5 ULN	Omit capecitabine until liver function recovers

Cardiotoxicity: Has been associated with fluoropyrimidine therapy (including myocardial infarction, angina, arrhythmias, cardiogenic shock, sudden death and ECG changes). Therefore, exercise caution in patients with prior history of coronary heart disease, arrhythmias or angina.

References: Glynne-Jones, R et al; Int J Radiation Oncol Biol Phys 2008; 72 (1): 119 - 126