PVI 5FU / MITOMYCIN C + RADIOTHERAPY

For locally advanced, unresectable pancreatic cancer

Drugs & Dosage:	Mitomycin C	7mg/m^2 (max 14mg) IV	D1 and D43 of radiotherapy
	5 Fluorouracil	**Prior to radiotherapy:**	300mg/m^2/24 hours} Continuous
		During radiotherapy:	200mg/m^2/24 hours} IV for
		After radiotherapy:	300mg/m^2/24 hours} 12 weeks

Radiotherapy: 54Gy in 27 fractions over 5½ weeks
The timing in relation to chemotherapy administration is not important.

Administration: Mitomycin C via fast running infusion 0.9% Sodium Chloride
5FU continuous IV via central venous catheter and ambulatory infusion device

Frequency: 5FU for a maximum of 12 weeks
Mitomycin C for 2 doses only – 1st dose on D1 of RT, and 2nd dose **6 weeks later** on Day 43
Radiotherapy (RT) start date is determined by waiting list.
Clinical review weekly whilst on RT

Main Toxicities: Myelosuppression; Diarrhoea; Mucositis / Stomatitis;
Palmar-Plantar Erythema (PPE); Coronary artery spasm (see Comments);
Haemolytic Uraemic Syndrome (see Comments); Ovarian failure/Infertility

Anti-emetics: Mildly emetogenic

Extravasation: Mitomycin C is a vesicant

Regular Investigations:		
	FBC	Weekly whilst on RT
	U&Es	Weekly whilst on RT as right kidney in field
	LFTs	3 weekly
	CEA	3 weekly
	Ca19-9	3 weekly
	MAG 3 scan	Before radiotherapy starts

Comments: Maximum cumulative dose 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.

Coronary artery spasm is a recognised complication of 5FU although the evidence base regarding aetiology, management and prognosis is not particularly strong. The incidence is estimated to be between 2% and 18%. Coronary artery spasm is more common in patients receiving continuous infusions of 5FU, and is usually reversible on discontinuing the infusion. Should a patient receiving 5FU present with chest pains, stop the 5FU. Standard investigation and treatment of angina may be required. If re-challenge is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, the 5FU should be withdrawn permanently.[1] Refer to Consultant to discuss.

Reason for Update: Warfarin statement removed/MMC renal info updated	Approved by Matron: I Patterson
Version: 2	Approved by Consultant: Dr Essapen
Supersedes: Version 1	Date: 19.9.05
Prepared by: S Taylor	Checked by: J Turner

Dose Modifications

Haematological Toxicity

WBC < 3.0 x 10^9/l
or
Neutrophils < 1.5 x 10^9/l
or
Platelets < 100 x 10^9/l

Delay all treatment for 1 week. Repeat FBC and, if within normal parameters, resume treatment at full dose.

Renal Impairment

NB. If serum creatinine increases by > 10% during RT, please liaise with Consultant on action to take, as part of right kidney is in the RT field (Dr. S. Essapen, Nov 2003).

The Cockcroft and Gault formula may be used to predict renal function before each Mitomycin C:

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

Hepatic Impairment

Moderate hepatic impairment	Reduce initial 5FU dose by 1/3
Severe hepatic impairment	Reduce initial 5FU dose by ½

Dose can be increased if no toxicity seen. If in doubt, check with the relevant Consultant.

Diarrhoea

Grade 1-2: Standard anti-diarrhoeal drugs can be used **but**, if diarrhoea persists, **stop** the 5 FU until resolved and recommence with a 25% dose reduction.

Cutaneous Toxicity

Patients with any grade PPE should receive Pyridoxine 50mg po tds throughout treatment. Sucralfate should be prescribed for stomatitis.
For Grade 3 mucositis or PPE, 5FU should be stopped for 1-2 weeks until healing has occurred and recommenced with a 25% dose reduction. Mitomycin C will continue at full dose.

References:
Maisey, N et al, 2002, JCO 20; (14): 3130 -3136
Shinchi, H et al, 2002, Int. J.Rad Oncol Biol. Phys., 53; (1):146 -150
[1]COIN Guidelines Oct 2000