E – CARBO – F

For use in Upper GI Cancer, in patients who are not eligible for entry into clinical trial, nor suitable for cisplatin or capecitabine

Drug/Dosage:	Epirubicin	50mg/m^2	IV	D1
	Carboplatin	AUC 5 (AUC3 if concerned – see Comments)	IV	D1
	5-Fluorouracil	200mg/m^2/24hrs	IV Continuous	D1 - D21

Administration: Epirubicin administered via fast running infusion of 0.9% Sodium Chloride
Carboplatin in 250ml of Glucose 5% over 30 minutes
5FU continuous via central venous catheter & ambulatory infusion device

Frequency: 3 weekly cycle for up to 6 cycles
Advanced / metastatic use: up to 6 cycles
All patients for full clinical review after 3 cycles - for locally advanced cases with no other assessable disease, a restaging OGD to assess mucosal response is required after Cycle 3.

Main toxicities: myelosuppression; thrombocytopenia; alopecia; mucositis; diarrhoea; plantar/palmar syndrome (PPE); cardiomyopathy; coronary artery spasm (see Comments); ovarian failure/infertility

Anti-emetics: Day 1: highly emetogenic
Continuous 5FU: mildly emetogenic

Extravasation: Epirubicin is a vesicant

Regular Investigations:	FBC	D1
	LFTs	D1
	U&Es	D1
	EDTA	Prior to 1st cycle
	MUGA scan	see Comments
	Restaging	after Cycle 3 (see Frequency)

Comments: Maximum cumulative dose Epirubicin = 950mg/m^2

Carboplatin dose should be calculated using the Calvert formula: Dose = Target AUC x (25+GFR)
If EDTA not yet available, Cockcroft and Gault may be used to predict GFR on Cycle 1, but dose must be corrected according to measured EDTA for the remaining cycles. EDTA should only be repeated if there is a 30% change in serum creatinine.

For patients with performance status 2 or who are considered at increased risk of neutropenia, consider giving carboplatin AUC 3 with dose escalation to AUC 5 if well tolerated.

A baseline MUGA scan should be performed where the patient is considered at risk of having significantly impaired cardiac contractility. If ejection fraction is less than 50%, an alternative regimen should be given. MUGA scan should be repeated if there is suspicion of cardiac toxicity at any point during treatment.

Reason for Update: Restaging requirements added / max no of cycles = 6	Approved by Lead Chemotherapy Nurse: C Palles-Clark
Version: 4	Approved by Consultant: Dr G Middleton
Supersedes: Version 3	Date: 1.4.08
Prepared by: S Taylor	Checked by: S Seymour

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.

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 Epirubicin and Carboplatin for 1 week. Continue with 5FU only if neutrophils ≥ 1.0 x 10^9/l and platelets ≥ 75 x 10^9/l. Repeat FBC after one week and, if normal, resume treatment at full dose.

If there is a 2 week delay, give all drugs at 75% dose.
If there is a > 2 week delay, give all drugs at 50% dose.

Renal Impairment: If EDTA or calculated CrCl < 20ml / min, carboplatin is contra-indicated.

Hepatic Impairment:

Bilirubin (µmol/l)	Epirubicin Dose
24 - 51	Give 50% dose
52 - 85	Give 25% dose
> 85	Omit

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.

5FU-Related Non-Haematological Toxicities: This includes diarrhoea, mucositis and palmar/plantar erythema.
Patients with any grade PPE should receive Pyridoxine 50mg po tds throughout remainder of treatment.
Standard anti-diarrhoeal drugs and mouthwashes should be used for symptomatic control.

For Grade 2 + toxicities, PVI 5FU should be discontinued until healing has occurred, and then recommenced with dose reduction indicated below:

Patient experienced Grade 2 toxicity:	Reduce 5FU dose by 50mg/m^2
Patient experienced Grade 3 toxicity:	Reduce 5FU dose by 100mg/m^2
Patient experienced Grade 4 toxicity:	**Discuss with Consultant before re-challenge.** Reduce 5FU dose by 150mg/m^2

Once a dose reduction has been made, all subsequent treatment should be given at the reduced dose.

References: Modified from MAGIC Trial, MRC 1999
[1]COIN Guidelines Oct 2000