EPIRUBICIN CISPLATIN FLUOROURACIL (ECF)

INDICATION (ICD10) D37

1. Unknown primary adenocarcinoma if appropriate (unlicensed)

PS 0, 1, 2

REGIMEN

Day 1	Prehydration	
	EPIRUBICIN	50mg/m^2 IV bolus
	FLUOROURACIL	200mg/m^2/24 hours continuous IV infusion over 7 days (start 4 hours before cisplatin on cycle 1)
	CISPLATIN	60mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours
	Posthydration	
Day 8	FLUOROURACIL	200mg/m^2/24 hours continuous IV infusion over 7 days
Day 15	FLUOROURACIL	200mg/m^2/24 hours continuous IV infusion over 7 days

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days up to 6 cycles

ANTI-EMETICS

Highly emetogenic day 1

Low emetogenic risk days 2 to 21

CONCURRENT MEDICATION REQUIRED

Cisplatin	Ensure adequate pre and post hydration. If urine output is <100ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.
Fluorouracil	Mouth and bowel support eg Loperamide, benzydamine mouthwash

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cisplatin – exfoliant

Epirubicin - vesicant

Fluorouracil - inflammitant

Central line (double lumen line required)

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs every day 1 only of each cycle

Neutrophils x 10^9/L ≥1.5

Platelets x 10^9/L ≥100

Ideally EDTA GFR should be used. Creatinine clearance calculated, at the Consultant's discretion.

Serum creatinine

ECG (possible ECHO) required if patient has preexisting cardiac disease

DPD test

Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Epirubicin	Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Fluorouracil	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function. Special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil. Stomatitis

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Cisplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Carboplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.
Fluorouracil	Cimetidine slightly increases exposure to fluorouracil Metronidazole increased toxicity Phenytoin concentration increased Warfarin

DOSE MODIFICATIONS

Epirubicin maximum lifetime dose
= 650mg/m^2 (in patients with cardiac dysfunction or exposed to mediastinal irradiation)
= 1000mg/m^2 (with normal cardiac function)

Haematological

Platelets $\geq 100 \times 10^9$/L Neutrophils $\geq 1.5 \times 10^9$/L	Give 100% dose
Platelets 50-100x10^9/L neutrophils 0.5-1.5x10^9/L	Stop fluorouracil, delay cisplatin and epirubicin until recovery. Restart fluorouracil and cisplatin at 100% dose, give 75% epirubicin dose on subsequent cycles
Platelets 25-49x10^9/L neutrophils <0.5x10^9/L	Stop fluorouracil, delay cisplatin and epirubicin until recovery. Restart fluorouracil and cisplatin at 100% dose, give 50% epirubicin dose on subsequent cycles
Platelets <25x10^9/L	Stop fluorouracil, delay cisplatin and epirubicin until recovery. Restart fluorouracil and cisplatin at 100% dose BUT omit epirubicin from subsequent cycles

Non-haematological

Cisplatin

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Fluourouracil

Diarrhoea and/or mucositis

Grade 2 toxicity – 1 week break from fluorouracil then restart at 150mg/m^2/day

Grade 3 toxicity – stop fluorouracil until symptoms resolve, then restart at 100mg/m^2/day

Grade 4 toxicity – stop fluorouracil until symptoms resolve, then restart at 50mg/m^2/day

Hepatic impairment

Epirubicin

Bilirubin 24-50micromol/L	give 50% dose
Bilirubin 51-85micromol/L	give 25% dose
Bilirubin >85micromol/L	omit

Fluorouracil

Significantly impaired hepatic function eg bilirubin >50micromol/L may be a sign of disease progression and require cessation of, or change in, treatment. Always discuss deteriorating liver function with consultant.

Bilirubin >85micromol/L	not recommended

Renal impairment

Cisplatin

CrCl >60ml/min	give 100% dose
CrCl 45-60ml/min	give 75% dose
CrCl <45ml/min	Not recommended, consider carboplatin AUC 4 or 5 every 4 weeks or switch to an appropriate oxaliplatin containing regimen

Epirubicin

CrCl severe renal impairment (GFR <30ml/min)	Dose reduce

Fluourouracil

CrCl >30ml/min	give 100% dose
CrCl <30ml/min	consider dose reduction

REFERENCES

1. Waters JS et al. Br J Cancer 1999; 80: 269-72