CISPLATIN FLUOROURACIL with concurrent RT (CF75)

INDICATION (ICD10) C15

1. Radical treatment oesophageal carcinoma (unlicensed). PS 0, 1, 2

REGIMEN

Day 1 Prehydration
CISPLATIN 75mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours
Posthydration
FLUOROURACIL 4000mg/m^2 over 96 hours via an infusor

CYCLE FREQUENCY AND NUMBER OF CYCLES

Cycles 1 and 2 - 3 weekly
Cycles 3 and 4 – 3-4 weekly, starting concurrently with RT

ANTI-EMETICS

Highly emetogenic day 1
Low emetogenic risk days 2, 3 and 4

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
Fluorouracil - inflammitant

Central line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Ideally EDTA GFR should be used
Creatinine clearance (GFR) calculated, at the Consultants discretion
Serum creatinine
DPYD (dihydropyrimidine dehydrogenase) 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.
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 (consider ECG at baseline). 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. Cisplatin 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

Haematological

If neutrophils <1.5x10^9/L and/or the platelet count <100x10^9/L delay the second course by one week, recheck blood count. Then if satisfactory (>1.5x10^9/L and >100x10^9/L) give 75% dose cisplatin and fluorouracil

If not satisfactory delay by a further week and recheck blood count, if satisfactory (>1.5x10^9/L and >100x10^9/L) then give 50% dose cisplatin and fluorouracil.

If still unsatisfactory after 2 week delay chemotherapy should be discontinued.

Non-haematological

Cisplatin

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

Hepatic impairment

Cisplatin

No need for dose adjustment

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.	
If hepatic function is impaired, the recommended dose can be reduced to give 50% to 70% dose, but no need for dose adjustment is expected in mild and moderate (without renal impairment).	
Bilirubin >85micromol/L	not recommended

Renal impairment

Cisplatin

CrCl >60ml/min	give 100% dose
CrCl 50-59ml/min	give 75% dose
CrCl 40-49ml/min	give 50% dose (curative intent) not recommended (palliative intent)
CrCl <40ml/min	not recommended or switch to an appropriate oxaliplatin containing regimen

Fluorouracil

If renal function is impaired, the recommended dose can be reduced to give 50% to 70% dose, but no need for dose adjustment is expected.

REFERENCES

1. J Clin Onc 1997; 5 (No 1): 277-284