CISPLATIN FLUOROURACIL (CF75)

INDICATION (ICD10) C21

1. Metastatic anal carcinoma (second line post MF) PS 0, 1, 2

REGIMEN

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

*Cisplatin dose may be decreased to 60mg/m^2

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 6 cycles

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 (single lumen)

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E including Mg^{++} and LFTs Neutrophils ≥1.5x10^9/L Platelets ≥100x10^9/L	baseline and every cycle
EDTA GFR or calculated CrCl at consultant's discretion.	baseline and every cycle
Serum creatinine	baseline and every cycle
DPYD (dihydropyrimidine dehydrogenase) test	baseline
Weight	baseline 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
DPYD variant identified follow national or local DPD dose modification guidelines.

Haematological

Neutrophils <1.5x10^9/L and/or platelets <100x10^9/L	delay treatment by 1 week then recheck blood count.
After 1 week delay	if counts recovered (neutrophils >1.5x10^9/L and platelets >100x10^9/L) give 75% dose cisplatin and fluorouracil. If counts not recovered delay by a further week and recheck blood count.
After 2 week delay	if counts recovered (neutrophils >1.5x10^9/L and platelets >100x10^9/L) give 50% dose cisplatin and fluorouracil. If counts not recovered 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	consider switch to an appropriate carboplatin or oxaliplatin containing regimen

Fluourouracil

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. ACT 2 trial. final protocol (v.1.20) 31/01/2002 Cancer research UK
2. COIN guidelines. Clin Oncol (R Coll Radiol), 2001. 13: pS211-248.

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Alternate cycles or team discretion
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E, calcium, magnesium & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
Dihydropyrimidine dehydrogenase (DPYD) deficiency test	X					This test is required for every patient newly started on capecitabine or fluorouracil. The result MUST be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary.
CT scan	X					Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle