CISPLATIN & PVI 5FU (CF) – ADVANCED USE

For use in relapsed squamous cell carcinomas of the cervix, vulva and vagina

Drugs/Dosage:	Cisplatin	60mg/m^2	IV	Day 1
	5-Fluorouracil	1000mg/m^2/24hrs	IV	Day 1 – Day 4
	Patients aged > 70 years:			
	Cisplatin	60mg/m^2	IV	Day 1
	5-Fluorouracil	750mg/m^2/24hrs	IV	Day 1 – Day 4

Administration:
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgSO_4$ IV over 2 hours
Mannitol 20% 100ml IV over 15 minutes
Cisplatin in 1 litre 0.9% sodium chloride IV over 2 hours
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgSO_4$ IV over 2 hours
500ml 0.9% sodium chloride IV **or** 500ml – 1 litre water orally over 1 hour

5FU continuous IV infusion over 4 days, given via CVC and ambulatory infusion device.

Frequency: 3 weekly cycle for 6 cycles

Main Toxicities: myelosuppression; alopecia; diarrhoea; mucositis; nephrotoxicity; neuropathy / ototoxicity; palmar/plantar erythema (PPE); coronary artery spasm (see Comments); ovarian failure/infertility

Anti-emetics: cisplatin: highly emetogenic; 5-fluorouracil: mildly emetogenic

Extravasation: non-vesicants

Regular Investigations:	FBC	Day 1
	U&Es & LFTs	Day 1
	Mg^{2+} and Ca^{2+}	Day 1
	EDTA	Prior to 1st cycle

Comments

For patients on Cycle 1 whose EDTA is not yet available, Cockcroft & Gault formula may be used to calculate creatinine clearance. Cisplatin dose should be adjusted if necessary once EDTA available. EDTA should only be repeated if the result is borderline at the start of treatment **or** if there is a 30% change in serum creatinine.

Check electrolytes – additional supplementation of potassium, calcium or magnesium may be required.

Ensure that patient is reviewed for side effects indicative of neurotoxicity or ototoxicity.

Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hr must be maintained throughout treatment, and cisplatin infusion should not be commenced unless this urine output is achieved. If the urine output is inadequate, the patient should be assessed and urine output increased by administering 500ml Sodium Chloride +/- furosemide 20 - 40mg. Furosemide 20 – 40mg po may also be given if there is a positive fluid balance of 1.5 litres, a weight gain of 1.5kg or symptoms of fluid overload. The patient should be asked to drink 2 litres

of fluid in the 24hrs following treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Coronary artery spasm is a recognised complication of 5FU although the evidence base regarding aetiology, management and prognosis is not particularly strong. Coronary artery spasm is more common in patients receiving continuous infusions of 5FU, which is usually reversible on discontinuing the infusion. Should a patient receiving 5FU present with chest pains, stop the 5FU. Standard investigation & treatment of angina may be required. If rechallenge 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	Delay treatment for 1 week.
	or	Repeat FBC. If normal, resume treatment at full dose.
	Neutrophils < 1.5 x 10^9/l	
	or	If there is a 2 week delay, give both drugs at 75% dose.
	Platelets < 100 x 10^9/l	If there is a > 2 week delay, give both drugs at 50% dose.

Renal Impairment: NB. Cisplatin is both eliminated primarily (> 90%) in the urine and is itself nephrotoxic.

GFR (ml/min)	Cisplatin Dose
≥ 60	Give 100% dose
45 - 59	Give 75% dose
44 – 20	Cisplatin contra-indicated Carboplatin AUC 5, administered in 250ml 5% Glucose over 30 minutes, may be substituted. It may be given according to this protocol, with however no requirement for pre- or post-hydration, nor fluid balance/urine monitoring
< 20	Carboplatin contra-indicated

Hepatic Impairment:

Moderate hepatic impairment	Reduce initial 5FU dose by 1/3
Severe hepatic impairment	Reduce initial 5FU dose by 1/2

Increase dose if no toxicity. If in doubt, check with relevant consultant.

Other Toxicities: If Grade 3/4 mucositis, diarrhoea or PPE occurs, give a 25% dose reduction for 5FU in subsequent cycles. Cisplatin will continue at full dose.
Patients with any grade PPE should receive pyridoxine 50mgs po tds throughout treatment.
If patient develops Grade 2 neuropathy or ototoxicity, discuss with Consultant.

References: Adapted from following studies:
O'Brien, M et al; Eur J Cancer B Oral Oncol (1994); 30B (4): 265 – 267
Ghaemmaghami, F et al; J Obstet Gynaecol (2003); 23 (4): 422 - 425
[1]COIN Guidelines Oct 2000