GEMCITABINE AND CISPLATIN

For metastatic or locally advanced inoperable pancreatic carcinoma – NICE approved

Drug/Dose:	Cisplatin	25mg/m^2	IV	D1, D8 and D15
	Gemcitabine	1000mg/m^2	IV	D1, D8 and D15

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 500ml 0.9% Sodium Chloride IV over 1 hour
Followed by: 500mls water orally over 1 hour, starting at the same time as:
Gemcitabine diluted in 250 ml 0.9% Sodium Chloride over 30 minutes

Frequency: Repeat every 28 days
Review prior to each cycle, and prior to Day 8/15 chemotherapy if there is a problem
Locally advanced: consider radiotherapy after 3 cycles
Metastatic: continue until progression, excessive toxicity or patient choice

Main Toxicities: myelosuppression; neuropathy; ototoxicity; nephrotoxicity; erythematous rash; peripheral oedema (mild-moderate & reversible); flu-like syndrome; ovarian failure/infertility

Anti-emetics: highly emetogenic

Extravasation: non vesicants

Regular Investigations:		
	FBC	D1, D8 & D15
	U&Es	D1, D8 & D15
	Mg^{2+} and Ca^{2+}	D1, D8 & D15
	LFTs	D1
	EDTA	Prior to 1st cycle
	CA 19-9	D1

Comments: For patients on Cycle 1 whose EDTA is not yet available, Cockcroft & Gault may be used to predict GFR. 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.

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 0.9% IV +/- 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.

Reason for Update: Renal & hepatic info added for gemcitabine	Approved by Lead Chemotherapy Nurse: C Palles-Clark
Version: 2	Approved by Consultant: Dr G Middleton
Supersedes: Version 1	Date: 25.6.07
Prepared by: S Taylor	Checked by: S Punter

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

Dose Modifications

Haematological Toxicity:

Day 1, Day 8 and Day 15:

Neutrophils		Platelets	Gemcitabine Dose	Cisplatin Dose
> 1.0 x 10^9/l	**and**	> 100 x 10^9/l	Give 100% dose	Give 100% dose
0.5 – 1.0 x 10^9/l	**or**	50 – 100 x 10^9/l	Give 75% dose	Give 75% dose
< 0.5 x 10^9/l	**or**	< 50 x 10^9/l	Defer 1 week	Defer 1 week

If a dose reduction to 75% has been made, then the doses should be increased to 100% on subsequent doses, providing the FBC is within normal limits.

Non-Haematological Toxicity:

For any Grade 3 – 4 toxicity, treatment should be deferred until recovery, and then continued with an appropriate dose reduction.

Renal Impairment:

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

GFR (ml/min)	Cisplatin Dose
> 60	Give 100%
50 – 60	Give 75%
40 – 50	Give 50%
< 40	CI (consider carboplatin)

If CrCl < 30ml/min, consider gemcitabine dose reduction – clinical decision

Hepatic Impairment:

If bilirubin > 27 µmol/L, initiate treatment with gemcitabine 800mg/m^2

Neurotoxicity:

Seek further advice if the patient reports symptoms indicative of neurotoxicity (paraesthesias, difficulty with motor control) or ototoxicity (tinnitus, deafness).

References:

Colucci, G et al; Cancer 2002; (94) 4: 902 - 910