GEMCITABINE AND CISPLATIN

Advanced or metastatic bladder cancer, ureteric cancer or renal pelvis carcinoma
Neo-adjuvant or adjuvant use in transitional cell carcinoma in high-risk, fit patients

Drug/Dose:	Gemcitabine	1000mg/m^2	IV	Day 1 and Day 8
	Cisplatin	70mg/m^2	IV	Day 1

Administration: **Gemcitabine** diluted in 250 ml 0.9% sodium chloride over 30 minutes

Cisplatin:
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 3 hours
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours
500ml 0.9% sodium chloride IV **or** 500ml -1 litre water orally over 1 hour

Frequency:
3 weekly cycle
Neo-adjuvant use: 3 – 4 cycles
Palliative use: 6 cycles
Adjuvant use: up to 6 cycles, at discretion of Consultant

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

Anti-emetics:
Day 1: highly emetogenic, including aprepitant
Day 8: mildly emetogenic

Extravasation: non vesicants

Regular Investigations:	FBC		Day 1 and Day 8
	U&Es		Day 1
	Mg^{2+} and Ca^{2+}		Day 1
	LFTs		Day 1
	EDTA		Prior to 1st cycle
	HCG, CEA,	}	Prior to Cycle 1, then repeat at each
	CA125, CA153,	}	cycle **only if raised at baseline**
	CA199	}	

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.

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

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.

Dose Modifications

Haematological Toxicity:

Day 1:

Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l — Delay treatment for 1 week. Repeat FBC and, if normal, proceed with treatment*.

*Reduce the gemcitabine dose for all subsequent cycles to 75% of the original cycle initiation dose if any of the following have occurred:

- Neutrophils < 0.5 x 10^9/l for > 5 days
- Neutrophils < 0.1 x 10^9/l for > 3 days
- Febrile neutropenia
- Platelets < 25 x 10^9/l
- Cycle delay of more than one week due to toxicity

Day 8:

Neutrophils		Platelets	Gemcitabine Dose
> 1.0 x10^9/l	**and**	> 100 x10^9/l	Give 100% of Day 1 dose
0.5 – 1.0 x10^9/l	**or**	50 – 100 x10^9/l	Give 75% of Day 1 dose
< 0.5 x10^9/l	**or**	<50 x10^9/l	Omit (do **not** defer)

If a dose reduction to 75% of the Day 1 dose has been made on Day 8, the dose should be increased to 100% again on Day 1 of the next cycle, providing the FBC has returned to normal limits.

Renal Impairment:

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

GFR (ml/min)	Cisplatin Dose
≥ 60	Give 100%
45 – 59	Give 75%
< 45	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 ototoxicity (tinnitus, deafness) or neurotoxicity (paraesthesias, difficulty with motor control).

References:

Von der Masse, H et al, JCO 2000; 18 (17): 3068 – 3077
Dash, A et al; Cancer 2008; 113: 2471 - 2477