GEMCITABINE AND CISPLATIN

An option for first-line use for advanced NSCLC - NICE Approved June 2001
Neo-adjuvant use in NSCLC – not NICE approved

Drug/Dose:	Gemcitabine	1250mg/m^2	IV	D1 and D8
	Cisplatin	80mg/m^2	IV	D1
	(Gemcitabine should be given prior to Cisplatin[1] on Day 1)			

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

Cisplatin: 1 litre 0.9% sodium chloride + 20 mmol KCl + 10 mmol $MgSO_4$ 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 sodium chloride 0.9% IV **or** 500mls – 1 litre water orally over 1 hour

Frequency: 3 weekly cycle:

- 4 cycles in palliative context is adequate, but for patients with impressive objective responses and excellent tolerability, consideration could be given to consolidating to a maximum of 6 cycles.
- For patients receiving sequential radiotherapy, 3 cycles should be given, followed by radiotherapy starting 3 weeks after Day 1 of Cycle 3. However, if there is a delay in starting RT, a 4th cycle should be given.
- For resectable disease, 3 – 4 cycles before surgery

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

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

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 supplements of magnesium, potassium or calcium 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 Day 1 dose has been made, then the dose should be increased to 100% for subsequent doses, providing the FBC has recovered to within normal parameters.

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:

Cortesi, E et al; Lung Cancer, Feb – Mar 2001; 31(2-3): 271-276
Crino, L et al; JCO, Nov 1999; 17 (11): 3522 – 3530
Van Zandwijk, L et al; JCO, July 2000; 18 (14): 2658-2664
[1]Shepherd, FA et al, Lung Cancer 2000; 30 (2): 117 – 125
Dosing schedule as Giaccone G et al; Seminars in Onc 2002; 29(3) supp 9: 47-49