VINORELBINE AND CISPLATIN

For use in advanced (Stage III and IV) NSCLC
Neo-adjuvant or adjuvant use in resectable NSCLC

*** Do not use this protocol if prescribing the chemo-radiotherapy regimen of vinorelbine, cisplatin & radiotherapy ***

Drugs/Dosage:	Vinorelbine	30mg/m^2	IV	Day 1 and Day 8
	Cisplatin	80mg/m^2	IV	D1

Administration: Vinorelbine diluted in 50ml 0.9% sodium chloride and infused over 5-10 minutes, running concurrently with 0.9% sodium chloride infusion.
Flush the vein afterwards with a further 250ml saline infusion at a free flowing rate.
(On Day 1, if at least 250ml of the cisplatin pre-hydration remains, this may be used as the flush instead)

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

Frequency: 3 weekly cycle, reviewed prior to each cycle
Adjuvant use: 4 cycles
Neo-adjuvant use before surgical resection: 3 – 4 cycles
Metastatic use: 4 cycles

Main Toxicities: myelosuppression; neurotoxicity; ototoxicity; alopecia (occasional)
constipation; nephrotoxicity; ovarian failure/infertility

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

Extravasation: Vinorelbine is a vesicant

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: If EDTA not yet available for patients on Cycle 1, use Cockcroft & Gault formula to predict GFR. Cisplatin dose should be adjusted if necessary on future cycles 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, calcium or potassium 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 and Day 8:

Neutrophils < 1.5 x 10^9/l	Delay treatment for 1 week. Repeat FBC and, if recovered, give 100% dose.
or	
Platelets < 100 x 10^9/l	If not, delay for a further week.

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%
20 – 44	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

Carboplatin dose should be calculated using the Calvert Formula:
Dose = Target AUC x (25 + GFR)

Hepatic Impairment: If ALT/AST > 5 x ULN and / or bilirubin > 2 x ULN, it is suggested that the vinorelbine dose be reduced by 33% and haematological toxicity closely followed up.

Neurotoxicity: Seek further advice if the patient reports symptoms indicative of neurotoxicity (paraesthesias, difficulty with motor control) or ototoxicity (tinnitus, deafness).
Treatment should be discontinued in the event of Grade 3 - 4 peripheral neuropathy or autonomic neuropathy causing constipation.

References:

International Adjuvant Lung Cancer Trial Collaborative Group; NEJM 2004; 350: 351 - 360
Wozniak, AJ et al, JCO 1998; Vol 16 (7): 2459-2465
Gebbia, V et al; Lung Cancer 2005; Vol 49 Supplement 2: 532
Tan, EH; Lung Cancer 2005; 49 (2): 233 – 240 (reference for carboplatin dosing)