Cisplatin and Etoposide (lung)

Indication

First line chemotherapy for patients with small cell lung cancer (SCLC), who have a good performance status (WHO PS 0-2).

Concomitant radiotherapy may start with cycle 2.

ICD-10 codes

Codes pre-fixed with C34

Regimen details

Day	Drug	Dose	Route
1	Cisplatin	75-80mg/m²	IV infusion
1	Etoposide	100mg/m²	IV infusion
2 and 3 **or**	Etoposide	100mg/m²	IV infusion
2 and 3	Etoposide	200mg/m²	PO

Cycle frequency

21 days

Number of cycles

4 - 6 cycles (usually 4)

Administration

Cisplatin is administered in 500mL sodium chloride 0.9% over 60 minutes following the pre and post hydration protocol below.

Infusion Fluid & Additives	Volume	Infusion Time
Sodium Chloride 0.9%	1000mL	1 hour
Mannitol 20% **OR** Mannitol 10%	200mL 400mL	30 minutes 30 minutes
Ensure urine output > 100mL / hour prior to giving cisplatin. Give a single dose of furosemide 20mg iv if necessary.		
Cisplatin	500mL	1 hour
Sodium Chloride 0.9% + 2g $MgSO_4$ + 20mmol KCl	1000mL	2 hours
TOTAL	**2700mL or 2900mL**	**4 hours 30 minutes**

Note: Patients with magnesium or potassium below the normal range should have 2g $MgSO_4$ and 20mmol KCl added to the pre-hydration bag and the duration of the infusion increased to 2 hours.

All patients must be advised to drink at least 2 litres of fluid over the following 24 hours.

IV etoposide is administered in 1000mL sodium chloride 0.9% and infused over a minimum of 1 hour.

Oral etoposide is available as 50mg and 100mg capsules. The dose should be rounded to nearest 50mg and swallowed whole on an empty stomach or an hour before food. In the event that the patient cannot swallow capsules, etoposide injection can be taken orally (diluted with orange juice immediately prior to administration) at a dose of 70% of the usual oral capsule dose. (This is an unlicensed use based on medical information from Bristol- Myers Squibb). Alternatively an additional IV dose may be given as above.
Note: oral absorption of etoposide is variable.

Pre-medication

Antiemetics as per local guidelines.

Emetogenicity

This regimen has severe emetic potential.

Additional supportive medication

If magnesium levels < normal reference range refer to local magnesium replacement guidelines.
Consider prophylactic ciprofloxacin 250mg BD and fluconazole 50mg OD for 7 days, starting on day 7, for patients with poor performance status or age >70 years.

Extravasation

Cisplatin is an exfoliant (Group 4)
Etoposide is an irritant (Group 3)

Investigations – pre first cycle

Investigation	**Validity period**
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period**
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days
Magnesium	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥1.5 x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine clearance	> 60mL/min
Bilirubin	≤1.5 x ULN
ALT/AST	≤1.5 x ULN
Alkaline phosphatase	≤2.5 x ULN

Dose modifications

- **Haematological toxicity**

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)		**Dose modification**
≥ 1.5	and	≥ 100		100%
< 1.5	or	< 100	1st occurrence	Delay treatment until recovery Resume with 100% dose and consider GCSF support
			Subsequent occurrences	Reduce doses as below
Febrile neutropenia or treatment delay for grade 4 neutropenia > 7 days	or	Grade 4 platelets requiring medical intervention or ≥ grade 2 bleeding with thrombocytopenia*	1st occurrence	100% dose and GCSF support or 80% dose
			2nd occurrence	70% dose
			3rd occurrence	Discontinue treatment

* Dose reductions rather than GCSF support would usually be required.

- **Renal impairment**

CrCl (mL/min)	**Cisplatin dose**	**Etoposide dose**
≥60	100%	100%
50-59	75%	100%
40-49	50% or switch to carboplatin AUC 5	75%
16-39	Contraindicated	75%
≤15	Contraindicated	50%

Carboplatin is contraindicated if CrCl <20mL/min

- **Hepatic impairment**

Bilirubin (x ULN)		**AST/ALT** (x ULN)	**Etoposide dose**
<1.5	and	< 1.5	100%
1.5-3.0	or	< 1.5-3.0	50%
>3.0	or	> 3.0	25% or omit (consultant decision)

No dose modification required for cisplatin.

- **Other toxicities**

If grade 3-4 neurotoxicity discontinue cisplatin and consider switching to carboplatin (discuss with consultant).

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Neurotoxicity
Nephrotoxicity
Ototoxicity

- **Frequently occurring side effects**

Myelosuppression
Constipation, diarrhoea
Stomatitis, mucositis
Alopecia
Nausea and vomiting

- **Other side effects**

Electrolyte disturbances
Fatigue

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.

Antibiotics: The renal toxicity of cisplatin is potentiated by aminoglycoside antibacterials (e.g. gentamicin) and amphotericin. Aminoglycosides should be avoided. If aminoglycosides are prescribed, close monitoring of renal function and serum antibiotic levels is required.

Avoid all nephrotoxic drugs where possible

Phenylbutazone, sodium salicylate and salicylic acid: can affect protein binding of etoposide.

Additional comments

References

- Summary of Product Characteristics Cisplatin (Hospira) accessed 25 Sept 2014 via www.medicines.org.uk
- Summary of Product Characteristics Etoposide (Hospira) accessed 25 Sept 2014 via www.medicines.org.uk
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.
- Skarlos, DV., et al. Randomised comparison on etoposide-cisplatin v etoposide-carboplatin in SCLC. Ann Onc. (1994) 5 (7) 601-607.

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Date: June 2015